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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

RIMFROST AS,
Petitioner,

v.

AKER BIOMARINE ANTARCTIC AS,
Patent Owner.

Case No. IPR2018-00295
Patent 9,320,765 B2

Before TINA E. HULSE, JACQUELINE T. HARLOW, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

SCHNEIDER, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

A. Background

Rimfrost AS ("Petitioner") filed a Petition requesting *inter partes* review of claims 1–48 of U.S. Patent No. 9,320,765 B2 ("the '765 patent"). Paper 1, ("Pet."). Aker Biomarine Antarctic AS ("Patent Owner") did not file a Preliminary Response. We determined, based on the information contained in the Petition that there was a reasonable likelihood that Petitioner would prevail in challenging claims 1–48 as unpatentable under 35 U.S.C § 103(a). Pursuant to 35 U.S.C. § 314, the Board instituted trial on June 14, 2018. Paper 9 ("Dec.").

Patent Owner filed a Response to the Petition on September 5, 2018. Paper 14 ("PO Resp."). Petitioner filed a Reply on November 26, 2018. Paper 19 ("Reply"). Patent Owner filed a Sur-Reply on January 18, 2019.[1] Paper 27 (Sur-Reply").

Patent Owner also filed a Motion to Amend on September 5, 2018. Paper 16 ("MTA"). Petitioner filed an Opposition to the Motion to Amend on November 26, 2018. Paper 20 ("MTA Opp."). Patent Owner filed a Reply on December 27, 2018. Paper 22 ("MTA Reply"). Petitioner filed a Sur-Reply to the Motion to Amend on February 1, 2019. Paper 30 ("MTA Sur-Reply").

On March 12, 2019, the parties presented arguments at an oral hearing. The hearing transcript has been entered in the record. Paper 34 ("Tr.").

[1] In an email to the Board dated January 3, 2019, the parties jointly requested authorization to file Sur-Replies in lieu of a Motion for Observations and Response to the Motion for Observations. The Board granted the request on February 4, 2019.

We have jurisdiction under 35 U.S.C. § 6. Petitioner bears the burden of proving unpatentability of the challenged claims, and that burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must prove unpatentability by a preponderance of the evidence. *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–48 of the '765 patent are unpatentable. We also find that the proposed amended claims are also unpatentable for the reasons that follow. *See* 35 U.S.C. § 316(e).

B. Additional Proceedings

The '765 patent was the subject of a now-terminated investigation before the International Trade Commission: *Certain Krill Products and Krill Meal for Production of Krill Oil Products*, Investigation No. 337-TA-1019. Pet. 2; Paper 4, 1; Ex. 1054.

The following proceedings before the Board involve the same parties as the instant *inter partes* review, and concern patents related to the '765 patent: IPR2017-00745 (Paper 24) (finding claims 1–20 of U.S. Patent No. 9,078,905 B2 ("the '905 patent") unpatentable); IPR2017-00746 (Paper 23) (finding claims 1–19 of U.S. Patent No. 9,028,877 B2 ("the '877 patent") unpatentable);[2] IPR2017-00747 (Paper 24) (finding claims 1–20 of the '905 patent not shown to be unpatentable); IPR2017-00748 (Paper 23) (finding claims 1–19 of the '877 patent not shown to be unpatentable);

[2] On October 12, 2018, Patent Owner filed Notices of Appeal seeking review of the final written decisions in IPR2017-000745 and IPR2017-000746. Paper 33, 5.

PGR2018-00033 (Paper 9) (declining to institute post grant review of claims 1–20 of U.S. Patent No. 9,644,170 B2); IPR2018-01178 (Paper 7) (instituting *inter partes* review of claims 1–32 of U.S. Patent No. 9,375,453 B2); IPR2018-01179 (Paper 7) (instituting *inter partes* review of claims 33–61 of U.S. Patent No. 9,375,453 B2); IPR2018-01730 (Paper 7) (instituting *inter partes* review of claims 1–20 of U.S. Patent No. 9,072,752 B1).

In addition, the ’877 and ’905 patents are at issue in *Aker Biomarine v. Olympic Holding AS*, Case No. 1:16-CV-00035 LPS-CJB (D. Del.), which has been stayed. Paper 33, 5.

C. The ’765 Patent (Ex 1001)

The ’765 patent, titled “Bioeffective Krill Oil Compositions” issued on April 26, 2016, from U.S. Patent Application No. 14/020,155, filed on September 6, 2013. Ex. 1001, at [54], [45], [21], [22]. The ’765 patent is a continuation of U.S. Patent Application No. 12/057,775, filed on March 28, 2008. The ’765 patent claims priority to U.S. Provisional Application No. 60/920,483, filed on March 28, 2007; U S. Provisional Application No. 60/975,058, filed on September 25, 2007; U.S Provisional Application No. 60/983,446, filed on October 29, 2007; and U.S. Provisional Application No. 61/024,072, filed on January 28, 2008. *Id.* at col. 1, ll. 6–14.

The ’765 patent describes extracts from Antarctic krill, small shrimp-like animals, that include bioactive fatty acids. Ex. 1001, col. 1, ll. 19–20. The ’765 patent teaches krill oil compositions characterized by having “high amounts of phospholipids, astaxanthin esters and omega-3 contents.” Ex. 1001, Abstract. According to the Specification, the compositions disclosed in the ’765 patent are effective “in a number of areas such as anti-inflammation, antioxidant effects, improving insulin resistances and improving blood lipid profile.” *Id.* In addition, the ’765 patent recognizes

that a myriad of health benefits have been attributed to krill oil in the prior art. For example, the '765 patent states that "[k]rill oil compositions have been described as being effective for decreasing cholesterol, inhibiting platelet adhesion, inhibiting artery plaque formation, preventing hypertension, controlling arthritis symptoms, preventing skin cancer, enhancing transdermal transport, reducing the symptoms of premenstrual symptoms or controlling blood glucose levels in a patient." *Id.* at col. 1, ll. 46–52.

The '765 patent acknowledges that krill oil compositions, including compositions having up to 60% w/w phospholipid content and as much as 35% w/w 5,8,11,14,17-eicosapentaenoic acid (EPA)/ 4,7,10,13,16,19-docosahexanoic acid (DHA) content, were known in the art at the time of the invention. *Id.* at col. 1, ll. 52–57. The '765 patent also indicates that supercritical fluid extraction with a solvent modifier was known to be a useful method for extracting marine phospholipids from salmon roe. *Id.* at col. 1, ll. 65–67.

According to the '765 patent, however, the solvent extraction methods used in the prior art to isolate krill oil from the krill "rely on the processing of frozen krill that are transported from the Southern Ocean to the processing site," which transportation is expensive and may result in the degradation of the krill starting material. *Id.* at col. 2, ll. 3–6. Such methods have included steps of placing the starting material into a ketone solvent, such as acetone, to extract the lipid soluble fraction, and recovering the soluble lipid fraction from the solid contents using a solvent such as ethanol. *Id.* at col. 1, ll. 32–40.

To overcome the above limitations, the '765 patent discloses "methods for processing freshly caught krill at the site of capture and

preferably on board a ship." *Id.* at col. 10, ll. 18–20. The '765 patent explains that the krill may be first subject to a protein denaturation step, such as a heating step, to avoid the formation of enzymatically decomposed oil constituents. *Id.* at col. 9, ll. 43–50; col. 10, ll. 26–31. Subsequently, the "oil can be extracted by an optional selection of nonpolar and polar solvents including use of supercritical carbon dioxide." *Id.* at col. 9, ll. 51–54.

In Example 7 of the '765 patent, "[k]rill lipids were extracted from krill meal (a food grade powder) using supercritical fluid extraction with co-solvent." *Id.* at col. 31, ll. 15–16.

> Initially, 300 bar pressure, 333°K and 5% ethanol (ethanol:CO2, w/w) were utilized for 60 minutes in order to remove neutral lipids and astaxanthin from the krill meal. Next, the ethanol content was increased to 23% and the extraction was maintained for 3 hours and 40 minutes. The extract was then evaporated using a falling film evaporator and the resulting krill oil was finally filtered.

Id. at col. 31, ll. 17–23.

Example 8 of the '765 patent discloses preparing krill oil using the same method described in Example 7, from the same krill meal used in that example. Ex. 1001, col. 31, ll. 44–46. The krill oil was then analyzed using ^{31}P NMR[3] analysis to identify and quantify the phospholipids in the oil. *Id.* at col. 31, ll. 47–49. Table 22[4] shows the phospholipid profiles for the raw material, the final product, and a commercially available krill oil, Neptune Krill Oil ("NKO"). *Id.* at col. 33, ll. 6–9. Table 22 is reproduced below:

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[3] Phosphorous Nuclear Magnetic Resonance.

[4] We view reference in the '765 patent to "table 25" (Ex. 1001, col. 32, ll. 7–10) to be an inadvertent typographical error, as the Specification does not include a table 25. We understand Example 8 of the Specification to refer, instead, to Table 22, which sets forth the described phospholipid profiles.

TABLE 22

Phospholipid profiles

	Type B krill powder	NKO	Krill Oil obtained in Example 7
PC	66.0	68.6	75.3
AAPC	12.0	7.0	13.0
PI			
1LPC	1.2	1.3	0.4
PS			
2LPC	7.4	13.8	2.9
LAAPC	2.2	1.2	0.9
PE	6.0	3.4	3.4
AAPE			1.5
SM			
GPC		1.3	
DHSM			
NAPE		3.4	
CL	5.3		2.1
LPE			0.5
LCL			
% PL in powder or lipid sample	8.3	30.0	47.9

Id. at col. 32, ll. 17–39.

The ’765 patent teaches that the “main polar ether lipids of the krill meal are alkylacylphosphatidylcholine (AAPC) at 7–9% of total polar lipids, lyso-alkylacylphosphatidylcholine (LAAPC) at 1% of total polar lipids (TPL) and alkylacylphosphatidyl-ethanolamine (AAPE) at <1% of TPL.” *Id.* at col. 32, ll. 10–16.

The ’765 patent teaches that the krill oil compositions can comprise a blend of lipid fractions obtained from krill. Ex. 1001, col. 2, ll. 62–63. The ’765 patent teaches

> In further embodiments, the present invention provides a blended krill oil composition comprising: from about 45% to 40 55% w/w phospholipids; from about 20% to 45% w/w triglycerides; and from about 400 to about 2500 mg/kg

> astaxanthin. In some embodiments, the blended krill oil product comprises a blend of lipid fractions obtained from *E. superba*. In some embodiments, the composition comprises 45 from about 25% to 30% omega-3 fatty acids as a percentage of total fatty acids and wherein from about 80% to 90% of said omega-3 fatty acids are attached to said phospholipids.

Id. at col. 5, ll. 39–48. The '765 patent also teaches that compositions of the invention can be formedby preparing an extract containing neutral lipids and another with polar lipids such as ether phospholipids and then blending the two extracts together. *Id.* at col. 12, ll. 3–36.

D. Illustrative Claim

Of the challenged claims, claims 1 and 25 are independent. Claims 2–24 depend from claim 1 and claims 26–48 depend from claim 25. Claim 1 is illustrative of the claimed subject matter and reads as follows:

> 1. A krill oil composition comprising *E. superba* krill oil suitable for oral administration, said krill oil comprising greater than about 3% ether phospholipids w/w of said krill oil; from about 27% to 50% non-ether phospholipids w/w of said krill oil so that the amount of total phospholipids in the composition is from about 30% to 60% w/w of said krill oil; from about 20% to 50% triglycerides w/w of said krill oil, and astaxanthan esters in amount of greater than about 100 mg/kg of said krill oil.

Ex. 1001, col. 34, l. 64–col. 35, l. 5. Claim 25 adds the additional limitation that the krill oil composition is encapsulated. Ex. 1001, col. 36, ll. 1–11.

E. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable on the following grounds. Pet. 7.

References	**Basis**	**Claims Challenged**
Sampalis[5], Catchpole[6], Fricke[7], and Breivik[8]	§ 103(a)	1–4, 7, 9–11, 14, 18–20, 25–28, 31, 33–35, 38, 42–44, and 47
Sampalis, Catchpole, Fricke, Breivik, and Bottino[9]	§ 103(a)	5, 6, 12, 13, 15, 16, 21–23, 29, 30, 36, 37, 39, 40, 45, and 46
Sampalis, Catchpole, Fricke, Breivik, and Randolph[10]	§103(a)	8, 17, 24, 32, 41, and 48

Petitioner also relies on the Declaration of Stephen J. Tallon, Ph.D. Ex 1006. Patent Owner relies on the declaration of Dr. Nils Hoem. Ex. 2001.

[5] Fotini Sampalis et al., *Evaluation of the Effects of Neptune Krill Oil™ on the Management of Premenstrual Syndrome and Dysmenorrhea,* 8 ALT. MED. 171–179 (2003) ("Sampalis") (Ex. 1012).
[6] Catchpole and Tallon, WO 2007/123424 A1, published Nov. 1, 2007 ("Catchpole") (Ex. 1009).
[7] Fricke et al. *Lipid, Sterol and Fatty Acid Composition of Antarctic Krill,* 19 LIPIDS 821–827 (1984) ("Fricke") (Ex. 1010).
[8] Harold Breivik, WO 2008/060163 A1, published May 22, 2008 ("Breivik") (Ex. 1037). Breivik claims priority to U.S. Provisional Application No. 60/859,289, filed Nov. 16, 2006 (Ex. 1037, [30]).
[9] N.R. Bottino, *The Fatty Acids of Antarctic Phytoplankton and Euphausiids. Fatty Acid Exchange among Trophic Levels in the Ross Sea,* 27 MARINE BIOL. 197–204 (1974) ("Bottino ") (Ex. 1007).
[10] Randolph et al., US 2005/0058728 A1, published Mar. 17, 2005 ("Randolph") (Ex. 1011).

II. ANALYSIS

A. Priority Date

Petitioner asserts that each claim of the '765 patent requires the presence of ether phospholipids, and that support for ether phospholipids was not introduced until the filing of U.S. Provisional Application No. 61/024,072 on January 28, 2008. Pet. 8–9.; Ex. 1006 ¶ 40. Petitioner thus contends "the earliest effective priority date for the claims of the '765 patent is no earlier than January 28, 2008." Pet. 8.

Alternatively, Petitioner argues that none of the applications to which the '765 patent claims priority include written description support for the open-ended ether phospholipid ranges recited in the challenged claims. *Id.* at 8–9. Petitioner thus asserts that the '765 patent is not entitled to a priority date earlier than the filing of the date of the application that issued as the '765 patent (i.e., September 6, 2013). *Id.*

Patent Owner does not contest Petitioner's assertion that the effective filing date of the '765 patent is no earlier than January 28, 2008. *See* PO Resp. 6.

We have reviewed the provisional applications that lead to the '765 patent and conclude that the earliest effective filing date of the claims of the '765 patent is no earlier than January 28, 2008. For purposes of this decision, we need not address whether the effective filing date of the claims of the '765 patent is later than January 28, 2008.

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 100(b) (2017); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016)

(affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings).[11] Under that standard, and absent any special definitions, we generally give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

1. Greater than about 5% w/w ether phospholipids

Claims 18 and 42 each recite the limitation calling for "greater than about 5% w/w ether phospholipids." Ex. 1001, col. 35, ll. 49–50, col. 36, ll. 59–61.

Petitioner contends the term "greater than about 5% w/w" should be construed to mean "greater than 4.5% w/w." Pet. 27. In support of this contention Petitioner contends that this is consistent with the Specification in that the Specification only recited whole numbers for weight amounts and that interpreting the term to extend down to 4.5% would be consistent with rounding to the next whole number. Pet. 26. Petitioner relies on Dr. Tallon's testimony that one skilled in the art would understand the term "about 5%" to extend down to 4.5% to support its position. Pet. 27 (citing Ex. 1002 ¶ 93).

[11] The Office recently changed the claim construction standard to be employed in an *inter partes* review. *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018). However, based on the filing date of the Petition in this proceeding, the applicable claim construction standard remains as set forth in 37 C.F.R. § 42.100(b) (2017).

Patent Owner contends that "greater than about 5%" should be construed to mean "greater than 4.95%." PO Resp. 12–13. In support of this contention, Patent Owner points to Dr. Tallon's testimony acknowledging that the values for phospholipids in Examples 7 and 8 of the '765 patent are accurate to a tenth of a percent. *Id.* at 12. Patent Owner argues that applying the rationale used by Dr. Tallon in his declaration, one skilled in the art would round a value of 4.95% up to 5% and 4.94% down to 4.9%. *Id.* at 13.

"Such broadening usages as 'about' must be given reasonable scope; they must be viewed by the decision maker as they would be understood by persons experienced in the field of the invention. Although it is rarely feasible to attach a precise limit to 'about,' the usage can usually be understood in light of the technology embodied in the invention." *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1554 (Fed. Cir. 1996).

After considering the parties' arguments and reviewing the Specification of the '765 patent, we conclude that Petitioner's proposed construction is consistent with the intrinsic evidence. Although the '765 patent does not explicitly address the issue of "about," the meaning of the term can be discerned from a careful reading of the Specification. Example 8 of the '765 patent reports the analysis of phospholipid fractions of a product of the invention and a commercially available Krill product. Ex. 1001, col. 31, l, 46–col. 32, l. 42. Table 22, reproduced above, reports the calculated values for the various phospholipids in values to a tenth of a percent. *Id.* at col. 32, ll. 18–38. In the discussion of the table, the values are rounded to the nearest whole number, not the nearest tenth. *Id.* at col. 32, ll. 11–15. This is consistent with the approach advanced by Petitioner.

For the purposes of this Decision, the term "greater than about 5% w/w" shall be construed to mean "greater than 4.5% w/w."

2. The remaining claims terms

Although both Petitioner, Pet. 18–24, and Patent Owner, PO Resp. 10–12, offer several claim constructions for additional terms, we determine that no explicit construction of any additional claim term is necessary for purposes of this Decision. In reaching this conclusion, we observe that Patent Owner does not contest Petitioner's proposed constructions of "plant phytonutrient" and "astaxanthin esters." PO Resp. 11. With respect to the remaining terms, the parties' proposed constructions are largely coextensive with each other, and to the extent those constructions differ, they do so in ways that do not impact our analysis. For example, our analysis below remains the same irrespective of whether we apply Petitioner's construction of "krill oil" as meaning "lipids extracted from krill," Pet. 19, or Patent Owner's interpretation, "mixture of lipids extracted from krill," PO Resp. 10.

C. Level of Ordinary Skill in the Art

The level of ordinary skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner asserts that a relevant skilled artisan would have possessed "an advanced degree in marine sciences, biochemistry, organic (especially lipid) chemistry, chemical or process engineering, or associated sciences" (Pet. 6), as well as having a complementary understanding of "organic chemistry and in particular lipid chemistry, chemical or process engineering,

marine biology, nutrition, or associated sciences; and knowledge of or experience in the field of extraction" (*id*.), in addition to "at least five years applied experience" (*id*.). Patent Owner has accepted this definition for purposes of this Proceeding. PO Resp. 13.

We agree with Petitioner and Patent Owner and find that Petitioner's description of the level of ordinary skill in the art at the time of invention of the '765 patent is consistent with the type of problems encountered in the art, prior art solutions to those problems, rapidity with which innovations are made, sophistication of the technology, and educational level of active workers in the field. *See In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). For purposes of this Decision, therefore, we adopt Petitioner's description. We also note that the applied prior art reflects a level of skill at the time of the claimed invention consistent with our determination. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

In addition, we recognize each of Petitioner's and Patent Owner's declarants as qualified to provide the proffered opinions on the level of skill and the knowledge of a person of ordinary skill in the art at the time of the invention. The relative weight that we assign such testimony, however, is subject to additional factors. *See, e.g.*, 37 C.F.R. § 42.65(a) ("Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight."); Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,763 (Aug. 14, 2012) (same).

D. Overview of the Prior Art

Petitioner relies on the combination of Sampalis, Catchpole, Fricke, Breivik, Bottino and/or Randolph to support its contention that claims 1–48 of the '765 patent would have been obvious. Pet. 7. Patent Owner asserts

that Prescott[12], Zimmerman[13], Calder[14], Zierenberg[15], Blank[16], Marathe[17], Hartvigsen[18], and Tanaka I[19] support its argument that an ordinarily skilled artisan would not have made Petitioner's proposed combinations and further that the prior art teaches away from encapsulation of krill oil with high levels of ether phospholipids. *See, e.g.*, PO Resp. 14–26. We provide an overview of each reference below.

1. Sampalis

Sampalis describes a clinical trial "[t]o evaluate the effectiveness of Neptune Krill Oil™ (NKO™) for the management of premenstrual syndrome and dysmenorrhea." Ex. 1012, 1. Sampalis explains that Neptune

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[12] Prescott et al., *Platelet-Activating Factor and Related Lipid Mediators,* 69 ANNU. REV. BIOCHEM. 419–45 (2000) ("Prescott") (Ex. 2003).
[13] Zimmerman et al., *The Platelet-Activating Factor Signaling System and Its Regulators in Syndromes of Inflammation and Thrombosis,* 30 CRIT. CARE MED. S294–301 (2002) ("Zimmerman") (Ex. 2004).
[14] P. Calder, *n-3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases,* 83 AM. J. CLIN. NUTR. 1505S–19S (2006) ("Calder") (Ex. 2005).
[15] Zirenberg and Grundy, *Intestinal absorption of polyenephosphatidylcholine in man,* 23 J. LIPID RES. 1136–1142 (1982) ("Zirenberg") (Ex. 2008).
[16] Blank et al., *Meats and Fish Consumed in the American Diet Contain Substantial Amounts of Ether-Linked Phospholipids,* 122 J. NUTR. 1656–61 (1992) ("Blank") (Ex. 2009).
[17] Marathe et al., *Inflammatory Platelet-activating Factor-like Phospholipids in Oxidized Low Density Lipoproteins Are Fragmented Alkyl Phosphatidylcholines,* 274 J. BIO CHEM. 28395–28404 (1999) ("Marathe") (Ex. 2011).
[18] Hartvigsen et al., *1-O-Alkyl-2-(ω-oxo)-sn-glycerols from Shark Oil and Human Milk Fat Are Potential Precursors of PAF Mimics and GBH,* 41 LIPIDS 679–693 (2006) ("Hartvigsen") (Ex. 2010).
[19] Tanaka et al., *Platelet-activating Factor (PAF)-like Phospholipids Formed during Peroxidation of Phosphatidylcholines from Different Foodstuffs,* 59 BIOSCI. BIOTECH. BIOCHEM. 1389–1393 (1995) ("Tanaka I") (Ex. 1014).

Krill Oil is "extracted from Antarctic krill also known as *E. superba*. *E. superba*, a zooplankton crustacean, is rich in phospholipids and triglycerides carrying long-chain omega-3 polyunsaturated fatty acids, mainly EPA and DHA, and in various potent antioxidants including vitamins A and E, astaxanthin, and a novel flavonoid." *Id*. at 4.

Sampalis discloses that each patient in the clinical trial was "asked to take two 1-gram soft gels of either NKO or omega-3 18:12 fish oil (fish oil containing 18% EPA and 12% DHA) once daily with meals during the first month of the trial." *Id*. Sampalis reports that "[t]he final results of the present study suggest within a high level of confidence that Neptune Krill Oil can significantly reduce the physical and emotional symptoms related to premenstrual syndrome, and is significantly more effective for the management of dysmenorrhea and emotional premenstrual symptoms than fish oil." *Id*. at 8.

2. Catchpole

Catchpole discloses "a process for separating lipid materials containing phospholipids" (Ex. 1009, 1, ll. 5–6) in order to produce a product containing "desirable levels of particular phospholipids" (*id*. at 3, ll. 27–28). Catchpole states that phospholipids "have been implicated in conferring a number of health benefits including brain health, skin health, eczema treatment, anti-infection, wound healing, gut microbiota modifications, anti-cancer activity, alleviation of arthritis, improvement of cardiovascular health, and treatment of metabolic syndromes. They can also be used in sports nutrition." *Id*. at 1, l. 29–2, l. 2. Catchpole further discloses that products having high levels of particular phospholipids "may be employed in a number of applications, including infant formulas, brain health, sports nutrition and dermatological compositions." *Id*. at 25, ll. 9–13.

Catchpole describes, in Example 18, the fractionation of krill lipids from krill powder using a process that employs supercritical CO_2 in a first extraction, and a CO_2 and absolute ethanol mixture in a second. *Id*. at 24, ll. 1–16. Table 16, reproduced below, reports the phospholipid concentrations present in the krill oil extract obtained by Catchpole.

Table 16

	Yield % of feed	Composition, %							
		PC	PI	PS	PE	CL	AAPC	AAPE	Other compounds
Feed		6.6	0.0	0.0	0.4	0.1	0.6	0.1	78.6
Extract 2	4.3	39.8	0.0	0.0	0.3	0.2	4.6	0.2	53.7
Residue	79.2	3.6	0.0	0.0	0.3	0.2	0.5	0.1	93.4

As shown in Table 16 above, the composition of Extract 2 includes 39.8% phosphatidylcholine ("PC"). *Id*. at Table 16. The ether phospholipids alkylacylphosphatidylcholine ("AAPC") and alkylacylphosphatidylethanolamine ("AAPE") were also present in Extract 2, representing 4.6% and 0.2%, respectively, of the extracted composition for a total of 4.8% ether phospholipids. *Id*.; Ex 1006 ¶¶ 145, 146. In addition, summing each of the reported phospholipid amounts reported for Extract 2 yields a total phospholipid concentration of 45.1%. Ex. 1006 ¶ 146.

3. Fricke

Fricke discloses the "lipid classes, fatty acids of total and individual lipids and sterols of Antarctic krill (*E. superba* Dana) from two areas of the Antarctic Ocean" as determined by thin layer chromatography, gas liquid chromatography, and gas liquid chromatography/mass spectrometry analyses. Ex. 1010, 1.

Table 1 of Fricke is reproduced below.

TABLE 1

Lipid Composition of Antarctic Krill
(*Euphausia superba* Dana)

Sample	12/1977	3/1981
Total lipid content (% wet weight)	2.7 ± 0.2	6.2 ± 0.3
Phospholipids		
Phosphatidylcholine	35.6 ± 0.1	33.3 ± 0.5
Phosphatidylethanolamine	6.1 ± 0.4	5.2 ± 0.5
Lysophosphatidylcholine	1.5 ± 0.2	2.8 ± 0.4
Phosphatidylinositol	0.9 ± 0.1	1.1 ± 0.4
Cardiolipin	1.0 ± 0.4	1.6 ± 0.2
Phosphatidic acid	0.6 ± 0.4	
Neutral lipids		
Triacylglycerols	33.3 ± 0.5	40.4 ± 0.1
Free fatty acids[a]	16.1 ± 1.3	8.5 ± 1.0
Diacylglycerols	1.3 ± 0.1	3.6 ± 0.1
Sterols	1.7 ± 0.1	1.4 ± 0.1
Monoacylglycerols	0.4 ± 0.2	0.9 ± 0.1
Others[b]	0.9 ± 0.1	0.5 ± 0.1
Total	98.9	99.3

Table 1 shows the total lipid content and the lipid composition data for the two krill samples analyzed by Fricke. *Id.* at 2. As indicated in Table 1, the krill samples respectively included approximately 33.3% ± 0.5% w/w and 40.4% ± 0.1% w/w triacylglycerols. *Id.*

4. Breivik

Breivik discloses the preparation of a lipid fraction from fresh krill. Ex. 1037, 1. Breivik discloses that krill oil obtained from Neptune Biotechnologies and Biosciences contains ≥ 40.0% phospholipids and ≥ 1.0 mg/g of esterified astaxanthin. *Id.* at 11.

5. Bottino

Bottino observes that "[t]he study of krill has become intensive in recent times, perhaps as a result of its potential importance as food," and explains that "[a] variety of organisms [are] usually included under that generic name, but in the Southern Oceans the name *E. superba* has been considered almost a synonym for krill." Ex. 1007, 1.

Bottino describes the fatty acid profiles for *E. superba*, *E. crystallorophias*, and phytoplankton. Ex. 1007, Abstract. Bottino explains that, in contrast to prior studies, lipids were extracted from *E. superba* "immediately after capture." *Id.* at 2. Euphausiids lipid extraction was performed "with a chloroform:methanol (2:1, v/v) mixture," as previously described by Folch, and the fatty acids were analyzed using chromatography. *Id.* at 1.

Table 1 of Bottino is reproduced below.

Table 1. *Euphausia superba*. Fatty acids (as weight per cent of total acids)

Fatty acid[a]	Station 8		Station 9	Station 11		
	Whole krill	HP+S[b]	Whole krill	Whole krill	HP+S	Remaining carcass
14:0	14.9	10.7	12.9	14.3	12.9	13.5
16:0	21.2	21.2	20.9	24.7	22.3	23.4
18:0	0.7	1.2	0.9	1.4	1.3	1.4
16:1(n-7)	9.0	6.7	10.7	8.9	8.2	8.0
18:1(n-9)	18.2	17.1	22.8	21.7	21.8	21.5
20:1(n-9)	0.6	0.9	1.1	0.9	1.2	1.1
18:2(n-3)	2.6	2.5	2.7	2.0	2.1	1.9
18:3(n-3)	1.1	1.2	1.4	1.0	1.0	1.1
18:4(n-3)	2.2	1.9	2.6	3.3	3.6	3.8
20:5(n-3)	16.0	22.2	11.8	11.4	13.9	11.6
22:6(n-3)	8.6	9.4	8.3	7.3	8.1	9.4
Minor fatty acids[c]	4.9	5.0	3.9	3.1	3.6	3.3

[a]The number preceding the colon gives the number of carbon atoms in the chain, the number following the colon the number of double bonds; (n-x): number of carbons in the chain minus number of carbons between the methyl end and the nearest double bond.

[b]Hepatopancreas plus stomach.

[c]Only those fatty acids present at a level of 1% or more are included.

Ex. 1007, Table 1. Table 1 discloses the fatty acid content of *E. superba* obtained from three different locations (i.e., stations) as a weight percent of total fatty acids. *Id.* at 2. Notably, only those fatty acids present at 1% or more as a weight percent of total fatty acids are included in Table 1. *Id.* Table 1

Table 3 of Bottino is reproduced below.

Table 3. Fatty acids of Antarctic phytoplankton and euphausiids (as weight per cent of total acids)

Fatty acid	Phytoplankton at Stations[a]												*Euphausia superba* (average of 3 stations)	*Euphausia crystallorophias* (average of 7 stations)
	8	9a	9b	11a	11b	13	14	15a	15b	15c	18a	18b		
8:0	–	–	–	0.4	–	1.2	1.0	–	–	0.7	–	–	–	
9:0	0.2	0.3	2.9	0.9	0.2	1.4	2.5	1.5	0.1	1.7	–	–	–	0.2
10:0	–	1.5	–	1.7	–	0.9	4.0	2.4	0.1	2.2	–	–	–	
11:0	–	–	–	0.7	1.3	1.2	1.9	1.1	trace	0.3	–	–	–	
12:0	1.3	2.3	2.3	1.9	0.4	2.0	2.2	2.5	0.4	0.8	0.2	–	0.2	0.1
13:0	–	1.1	–	–	–	0.4	3.0	0.8	–	–	–	–	–	0.1
14:0	9.7	22.5	11.5	15.9	22.9	25.5	20.7	17.4	19.3	5.1	13.0	9.5	14.0	2.4
15:0	1.9	0.3	1.6	2.6	1.7	2.6	–	3.4	0.7	1.1	0.3	–	0.4	0.1
16:0	20.4	20.1	19.9	16.0	18.8	21.7	18.5	18.7	17.2	16.1	17.3	14.9	22.3	14.6
18:0	7.0	2.1	3.3	2.0	2.0	2.6	2.2	1.9	1.8	5.2	1.7	1.5	1.0	0.5
10:1(n-?)	0.6	2.2	2.5	–	0.8	–	–	–	–	–	0.2	–	–	–
11:1(n-?)	–	–	–	0.7	–	1.9	2.0	1.3	0.1	0.9	–	–	–	–
12:1(n-?)	–	2.8	1.5	1.6	2.4	0.7	1.2	1.6	0.2	0.9	1.5	0.3	–	–
13:1(n-?)	–	0.5	–	1.0	–	0.6	1.8	1.4	0.1	1.1	–	–	–	–
15:1(n-?)	0.5	0.7	0.6	1.3	0.6	1.2	1.0	2.7	0.4	0.7	1.8	–	trace	–
16:1(n-?)	12.4	8.3	7.5	6.2	5.7	5.3	3.4	7.8	3.6	3.2	13.1	10.3	9.5	7.9
17:1(n-?)	1.6	0.3	0.9	0.6	0.3	0.2	–	0.3	0.3	trace	1.4	0.9	0.5	0.3
18:1(n-9)	12.1	16.0	15.6	16.2	18.3	16.3	24.8	11.4	20.2	12.5	17.3	18.7	20.8	46.2
20:1(n-9)	0.4	–	0.8	trace	–	1.7	–	0.1	trace	–	0.3	0.3	0.9	0.2
18:2(n-6)	2.1	0.1	0.3	0.2	0.1	–	–	–	0.1	–	4.1	3.8	0.2	–
18:2(n-3)	3.7	3.3	2.4	3.1	3.3	3.0	2.7	2.1	7.1	12.0	1.2	1.7	2.4	2.1
22:2(n-6)	–	–	–	–	–	0.8	0.9	1.6	2.0	–	–	–	–	–
22:2(n-3)	–	0.6	0.7	1.4	1.4	–	–	–	–	–	–	–	–	–
18:3(n-6)	0.3	0.3	0.3	0.2	0.2	–	–	–	0.2	0.3	0.2	0.3	0.2	0.1
18:3(n-3)	0.9	0.7	0.6	0.7	0.7	0.7	0.3	0.2	0.1	0.2	0.2	0.3	1.2	0.9
20:3(n-6)	0.4	0.2	–	trace	0.9	trace	–	0.3	2.6	0.1	–	0.1	–	–
20:3(n-3)	0.2	0.2	0.3	–	–	–	–	trace	0.9	1.0	–	0.2	0.5	0.3
16:4(n-1)	–	–	0.5	–	–	–	–	–	–	6.3	–	–	–	–
18:4(n-3)	2.0	3.1	3.5	5.2	6.0	3.0	2.7	3.2	6.2	0.9	2.2	2.5	2.7	1.2
20:4(n-6)	–	–	–	0.4	–	–	–	–	–	4.7	–	–	0.4	0.4
20:4(n-3)	0.2	–	0.3	0.2	–	–	–	0.1	trace	–	–	0.2	0.4	0.1
22:4(n-6)	–	–	–	–	–	–	–	–	–	trace	–	–	0.2	–
22:4(n-3)	1.3	–	trace	–	–	–	–	trace	–	trace	–	–	–	–
20:5(n-3)	11.4	4.8	9.2	7.0	6.4	1.7	2.1	5.3	6.0	2.1	18.4	23.4	13.1	14.4
22:5(n-6)	1.1	–	–	–	–	–	–	–	–	–	–	–	–	–
22:5(n-3)	0.3	0.3	–	–	–	–	–	0.1	–	2.1	–	–	0.2	–
22:6(n-3)	6.1	4.9	7.9	8.4	5.5	0.9	0.8	7.1	7.8	16.5	5.5	11.0	8.1	7.5
Minor fatty acids[b]	3.3	1.5	4.3	4.6	1.0	3.2	0.6	4.0	2.8	1.8	0.5	0.9	0.8	0.4

[a] Microscopic examination indicated that the following genera predominated in each station. Station 9: *Eudorina, Pandorina;* Station 10: *Thalassiosira, Fragilaria, Nitzchia, Corethron,* Silicoflagellates; Station 11: *Corethron, Fragilaria, Chaetoceros,* Silicoflagellates; Station 12: *Corethron, Fragilaria, Nitzchia,* Tintinnids; Station 13: Complex mixture; Station 14: *Phaeocystis;* Station 15: *Phaeocystis, Chaetoceros, Nitzchia, Thalassiosira, Fragilaria;* Stations 17 and 18: *Fragilaria, Nitzchia, Coscinodiscus,* Dinoflagellates, Tintinnids.

[b] Only those fatty acids present at a level of 1% or more are included. See footnotes to Tables 1 and 2 for further explanation.

Ex. 1007, Table 3. Table 3 reports the identity and average amount of each fatty acid present in the *E. superba* samples analyzed as a weight percentage of total fatty acids.

6. Randolph

Randolph discloses compositions for modulating cytokines to regulate an inflammatory or immunomodulatory response including, inter alia, rosehips and krill oil. Ex. 1011 ¶ 8. With regard to rosehips, Randolph discloses that the composition may include one or more rosehip ingredients, such as "dried rosehips, rosehip oil, and rosehip extracts." *Id.* ¶ 24. Concerning krill oil, Randolph discloses that

> [a] composition of the invention can include krill oil. Krill oil can be obtained from any member of the E. family, for example E. superba. Conventional oil producing techniques can be used to obtain the krill oil. In addition, krill oil can be obtained commercially from Neptune Technologies and Bioresources of Quebec, Canada.

Id. ¶ 39. Randolph further explains that "[a] composition can contain any amount of krill oil," but will typically contain "between about 300 mg and about 3000 mg of a krill oil ingredient." *Id.* ¶ 40.

Randolph teaches:

> A composition can contain any amount of an astaxanthin ingredient. For example, at least about 1 percent (e.g., at least about 2, 3, 4, 5, 10, 15, 20, 25, 30, 35, 40, 50, 60, 70, 80, or 90 percent) of a dietary supplement can be astaxanthin. Typically, a composition contains between about 0.5 mg and about 50 mg of an astaxanthin ingredient.

Id. ¶ 44.

Randolph also discloses that "[t]he ingredients of the composition can be processed into forms having varying delivery systems. For example, the ingredients can be processed and included in capsules, tablets, gel tabs, lozenges, strips, granules, powders, concentrates, solutions, lotions, creams

or suspensions." Ex. 1011 ¶ 46. Randolph further discloses that "[a] soft gel capsule of the composition can be manufactured to include krill oil. This capsule can be manufactured using conventional capsule manufacturing techniques. The amount of krill oil in each capsule is about 300 mg." *Id.* ¶ 52.

7. Prescott

Prescott discloses that Platelet Activating Factor ("PAF") "is a phospholipid with potent, diverse physiological actions, particularly as a mediator of inflammation." Ex. 2003, Abstract. Prescott explains that

> [t]he PAF receptor recognizes the sn-1 ether bond of PAF, its short sn-2 acetyl residue, and the choline head group; alteration of any of these structures greatly decreases signaling through the PAF receptor. Extension of the sn-2 acetyl residue by one methylene is without consequence, but extension by two methylenes decreases activity by a factor of 10- to 100-fold, depending on the assay. Extension beyond this results in the loss of signaling through the PAF receptor.

Ex. 2003, 13 (internal citations omitted).

Prescott further discloses that "[o]xidation of complex lipids in reduced systems has defined potential oxidation pathways and products, but whether such oxidizing conditions exist in vivo is problematic, given the unstable nature of the reactive intermediates and the potential of metabolism of the oxidation products." Ex. 2003, 14.

8. Zimmerman

Zimmerman is a review article that teaches that "[t]he PAF signaling system can trigger inflammatory and thrombotic cascades, amplify these cascades when acting with other mediators, and mediate molecular and cellular interactions (cross talk) between inflammation and thrombosis." Ex. 2004, Abstract. Zimmerman explains that artificial oxidation of

phosphatidylcholines "generates a large series of phospholipids in which the polyunsaturated fatty acid at the sn-2 position . . . is fragmented to shorter chain lengths. Some of these oxidized phospholipids have sufficiently short sn-2 residues and other structural features that allow them to be recognized by the PAF receptor." *Id.* at 4–5.

9. Calder

Calder is a review article discussing the effects of polyunsaturated fatty acids on inflammation. Ex. 2005, Abstract. Calder discloses that at "sufficiently high intakes, long-chain n-3 polyunsaturated fatty acids (PUFAs), as found in oily fish and fish oils, decrease the production of inflammatory eicosanoids, cytokines, and reactive oxygen species and the expression of adhesion molecules." *Id.* Calder reports that fish oil containing PUFAs has been shown to be effective in treating rheumatoid arthritis. *Id.* at 1511S. PAFs are found in the synovial fluid of patients with rheumatoid arthritis. *Id.*

10. Zierenberg

Zierenberg reports a study to determine the absorption of phosphatidylcholine in the intestine. Ex. 2008, 1136. Zierenberg reports that at least a portion of phosphatidylcholine administered orally is absorbed by the small intestine. *Id.*

11. Blank

Blank reports a study to determine the amounts of ether-containing phospholipids found in common foods. Ex. 2009, Abstract. Blank discloses that ingestion of phospholipids could contribute to the production of platelet activating factor. *Id*. While Blank reports that ether-linked phospholipids were found in all the samples tested, Blank also states, "Whether and to what extent these levels of dietary ether phospholipids would affect the production of, and subsequent biological responses induced by, PAF in humans are presently unknown." *Id.* at 1660–61.

12. Hartvigsen

Hartvigsen reports a study to determine if the peroxidation and lipolysis of 1-O-alkyl-2,3-diacyl-sn-glycerols ("DAGE") are a potential source of precursors of PAFs mimics. Ex. 2010, Abstract. Hartvigsen discloses it is possible that PAF mimics can be formed from DAGE. *Id.*

13. Marathe

Marathe reports a study relating to the production of PAFs from the oxidation of synthetic phosphatidylcholine. Ex. 2011, Abstract. Marathe focused on short-chain alkyl phosphatidylcholine such as C_4 analogs and homologs. *Id.* at 28401. Marathe teaches that "The PAF receptor shows a several hundredfold selectivity for the sn-1 ether bond of PAF, and complete specificity for the sn-2 acetyl residue compared with the long chain fatty acyl residue of most alkyl phosphatidylcholines (5, 6)." *Id.* at 28395.

14. Tanaka

Tanaka examines the "PAF-like lipids formed during peroxidation of PCs from hen egg yolk, salmon roe, sea urchin eggs, and krill in an FeSO4/EDTA/ascorbate system." Ex. 1014, Abstract. Tanaka discloses the phosphatidylcholine subclasses, and their relative amounts, present in

Antarctic krill (E. superba) extract. *Id.* at 1390–91. Tanaka explains that phosphatidylcholine was purified from crude krill lipid extract using column chromatography and thin layer chromatography. *Id.* at 1390. Successive degradations of the purified extract using alkaline and acid hydrolysis were then performed to measure the percentages of phosphatidylcholine subclasses in the extract. *Id.*

Table 1 of Tanaka is reproduced below.

Table I. Subclass Composition of PCs from Food Stuffs

PC	Diacyl	Alkylacyl	Alkenylacyl
		%	
Hen egg yolk	99.2±0.2	0.8±0.1	<0.1
Salmon roe	98.8±0.2	1.2±0.2	<0.1
Sea urchin egg	57.5±1.1	41.5±0.3	1.0±0.8
Krill	77.0±1.2	23.0±1.2	<0.1

Values are means±SE for four experiments.

Id., Table 1. Table 1 shows that the ether phospholipid AAPC accounted for 23.0% +/- 1.2% of the total phosphatidylcholine present in Antarctic krill extract. *Id.* at 1391.

Tanaka concludes that although the study "demonstrated the formation of PAF-like phospholipids during peroxidation of PCs from different foodstuffs[,] . . . the occurrence of PAF-like lipids in some stored foods is still speculative and requires further investigation." *Id.* at 1393.

E. Obviousness Based on Sampalis, Catchpole, Fricke and Breivik

Petitioner asserts that claims 1–4, 7, 9–11, 14, 18–20, 25–28, 31, 33–35, 38, 42–44, and 47 are unpatentable under 35 U.S.C. § 103(a) as obvious over Sampalis combined with Catchpole, Fricke, and Breivik. Pet. 28–47. Patent Owner disagrees. PO Resp. 14–29.

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and, where presented, (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17–18.

"An obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *CRFD Research, Inc. v. Matal*, 876 F.3d 1330, 1340 (Fed. Cir. 2017) (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–1368 (Fed. Cir. 2016)).

In assessing whether an ordinarily skilled artisan would have had reason to combine known elements in order to arrive at the claimed invention, it will often "be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design

community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art." *KSR*, 550 U.S. at 418.

A reference may be said to teach away from such combination "when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the [patentee]." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009) (quoting *Ricoh Co. v. Quanta Comput. Inc.*, 550 F.3d 1325, 1332 (Fed. Cir. 2008)). In analyzing whether a reference teaches away from the claimed invention, that reference "must [be] considered for all it taught, disclosures that diverged and taught away from the invention at hand as well as disclosures that pointed towards and taught the invention at hand." *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 296 (Fed. Cir. 1985) (citation omitted). A reference does not teach away "if it merely expresses a general preference for an alternative invention but does not 'criticize, discredit, or otherwise discourage' investigation into the invention claimed." *DePuy*, 567 F.3d at 1327 (quoting *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004)). Even if a reference is not found to teach away, however, its statements regarding preferences are relevant to a finding regarding whether a skilled artisan would be motivated to combine that reference with another reference. *See Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1051 n.15 (Fed. Cir. 2016) (en banc) (noting that, even if a reference "does not teach away, its statements regarding users preferring other forms of switches are relevant to a finding regarding whether a skilled artisan would be motivated to combine the slider toggle in" that reference with the invention of a second reference).

"The reasonable expectation of success requirement refers to the likelihood of success in combining references to meet the limitations of the claimed invention." *Intelligent Bio-Sys., Inc.*, 821 F.3d at 1367. A reasonable expectation of success "does not require absolute predictability of success . . . *all that is required is a reasonable expectation of success*." *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (quoting *In re O'Farrell*, 853 F.2d 894, 903–904 (Fed. Cir. 1988)). "What does matter is whether the prior art gives direction as to what parameters are critical and which of many possible choices may be successful." *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 965 (Fed. Cir. 2014).

Petitioner contends that Sampalis teaches the oral administration of an effective amount of encapsulated krill oil in the form of a soft gel. Pet. 29; Ex. 1006 ¶¶ 101, 102; Ex. 1012, 4. In support of this position, Petitioner's declarant, Dr. Tallon, testifies that Sampalis teaches that krill oil "was also found to be safe and effective for oral administration." Ex. 1006 ¶ 205.

Petitioner asserts that Catchpole teaches a krill oil extract comprising greater than about 3% ether phospholipids w/w of the krill oil extract, from about 27% to about 50% non-ether phospholipids and that the total phospholipids in the krill oil composition is about 30 to 60% w/w of the krill oil composition. Pet. 30–32. In this regard, Petitioner points out that Catchpole expressly describes, in Table 18, a krill extract having 4.8% ether phospholipids, including 4.6% AAPC and 0.2% AAPE, and a total phospholipid content of 45.1%. Pet. 31–32; Ex. 1006 ¶¶ 144–145; Ex. 1009, 24, ll. 1–19, Table 16. Petitioner also points to the testimony of Dr. Tallon where he concludes that subtracting the percent of ether phospholipids reported in Catchpole, 4.8%, from the total phospholipid content reported in

Catchpole, 45.1, yields a non-ether phospholipid content of 40.3%. Pet. 32; Ex. 1006 ¶¶ 145, 146, 281, 282.

Petitioner also asserts that Fricke teaches a krill oil composition that includes from about 20% to about 50% triglycerides w/w of the krill oil. Pet. 32. In support of this assertion, Petitioner points to Table I of Fricke, which reports the lipid compositions of two Antarctic krill samples. Pet. 32; Ex. 1010, 2. Fricke reports the level of triglyceride for the 1977 sample as 33.3% ± 0.5 and for the 1981 sample as 40.4% ± 0.1. Pet. 32; Ex. 1006 ¶¶ 167, 168, 281, 283; Ex. 1010, 2, Table I.

With respect to the astaxanthin ester content, Petitioner contends that Breivik discloses a krill oil composition containing greater than about 100 mg astaxanthin per kg of krill oil. In support, Petitioner points to page 11 of Breivik, which discloses the components of the lipid fraction of a known krill oil, which includes ≥ 1.0 mg/g of esterified astaxanthin. Pet. 34–35; Ex. 1006 ¶ 130; Ex 1037, 11.

According to Petitioner, it would have been obvious to a person of ordinary skill in the art to combine the krill oil composition disclosed in Catchpole, Fricke, and Breivik with the mode of administration taught by Sampalis to create a krill oil suitable for oral administration and having the health benefits disclosed by Sampalis, Catchpole, and Breivik. Pet. 42–46; Ex. 1006 ¶¶ 50–54, 115, 139–140, 200–203. Petitioner further asserts that a relevant skilled artisan would have had reason to use the krill extract taught by Catchpole in the mode of administration taught by Sampalis because Catchpole describes an array of processing and consumer benefits that derive from the disclosed supercritical fluid extraction method. Pet. 43–44; Ex. 1006 ¶¶ 137–140. In particular, Petitioner explains that extracts prepared according to Catchpole are "considered to be more 'natural' than

extracts produced using other solvents" (Pet. 43 (citing Ex. 1009, 2, ll. 18–25)), and that "Catchpole discloses that it is an object of the invention described therein to provide a process for producing a product that contains desirable levels of particular phospholipids" (*id*. (citing Ex. 1009, 3, ll. 27–29)).

In addition, Dr. Tallon testifies that the lipid components described in the claims of the '765 patent "are the natural lipid components in the *E. superba* krill oil that can be extracted using any of a number of suitable solvents" (Ex. 1006 ¶ 286), and that the relative proportions of those lipid components "can also be varied in a predictable way by applying a combination of solvents with different polarity to selectively concentrate and blend groups of compounds based on their different solubility" using methods and solvents that would have been well known by a relevant skilled artisan (*id*.), indicating that an ordinarily skilled artisan would have had a reasonable expectation of success in making the proposed combination.

Having reviewed the cited evidence, and the record as a whole, we find that Petitioner has accurately described the above-stated teachings of Sampalis, Catchpole, Fricke, and Breivik, which we adopt as our own. *See* Pet. 28–47. Indeed, Patent Owner does not challenge Petitioner's assertion that Catchpole and/or Sampalis discloses each element of challenged claims 1–4, 7, 9–11, 14, 25–28, 31, 33–35, and 38. Instead, the parties' dispute with respect to these claims centers upon whether an ordinarily skilled artisan would have had reason to combine Sampalis, Catchpole, Fricke and Breivik.

With respect to claims 18–20, 42–44 and 47, Patent Owner presents an additional argument that none of the references teach or suggest a krill oil

composition having greater than about 5% w/w ether phospholipids. Thus, our following analysis focuses on these issues.

1. *Rationale to Combine and Reasonable Expectation of Success*

With respect to claims 1-4, 7, 9-11, 14, 18-20, 25-28, 31, 33-35, 38, 42-44, and 47 Petitioner contends that a person of ordinary skill in the art would have sought to combine the ether phospholipid-containing krill oil extract of Catchpole with the mode of administration (encapsulated gel caps) taught by Sampalis in order to formulate a krill oil dosage form including an effective amount of krill extract and having the health benefits disclosed by Catchpole and Sampalis. Pet. 32–33; Ex. 1006 ¶¶ 28–32, 193–195. Petitioner asserts that a relevant skilled artisan would have had reason to use the krill extract taught by Catchpole in the mode of administration taught by Sampalis because Catchpole describes an array of processing and consumer benefits that derive from the disclosed supercritical fluid extraction method. Pet. 32–34; Ex. 1006 ¶¶ 193–195. According to Petitioner, the solvent-free extracts produced by Catchpole are "considered to be more 'natural' than extracts produced using other solvents." *Id.* at 33 (citing Ex. 1006 ¶ 83; Ex. 1009, 2:18–25). In addition, Petitioner represents that "Catchpole details a host of health benefits obtained from the administration of phospholipids, including ether phospholipid compositions extracted from krill," and "discloses that it is an object of the invention described therein to provide a process for producing a product that contains desirable levels of particular phospholipids." *Id*. (citing Ex. 1006 ¶¶ 84–86; Ex. 1009, 3:27–29).

In view of these teachings by Catchpole, and the disclosure by Sampalis that encapsulated *E. superba* krill oil extract is useful to treat inflammatory conditions, including premenstrual syndrome and

dysmenorrhea, Petitioner reasons that an ordinarily skilled artisan would have sought to include the more "natural" extract of Catchpole in the soft gel krill oil capsule taught by Sampalis. Pet. 33–34 (citing Ex. 1006 ¶¶ 28–32, 200, 201; Ex. 1012, 4).

In addition, Petitioner's declarant, Dr. Tallon, testifies that the lipid components described in the claims of the '765 patent "are the natural lipid components in the krill oil that can be extracted using any of a number of conventional solvents" (Ex. 1006 ¶ 31), and that the relative proportions of those lipid components "could be varied in predictable ways by applying a single solvent or combination of solvents including super critical fluid extraction to selectively extract specific groups of lipid components based on their different solubility" using methods and solvents that would have been well known by a relevant skilled artisan (*id*.), indicating that an ordinarily skilled artisan would have had a reasonable expectation of success in making the proposed combination. *Id.*

Based on our review of the record as presented, we determine that a preponderance of the evidence supports Petitioner's contention that an ordinarily skilled artisan would have had reason for, and a reasonable expectation of success in, combining Catchpole and Sampalis to arrive at the claimed invention.

Catchpole teaches that phospholipids confer a number of health benefits including "brain health, skin health, eczema treatment, anti-infection, wound healing, gut microbiota modifications, anti-cancer activity, alleviation of arthritis, improvement of cardiovascular health, and treatment of metabolic syndromes." Ex. 1009, 1. Catchpole also teaches that a composition having greater than 5% acylalkyphospholipids is preferred. *Id.* at 9. In addition, we credit Dr. Tallon's testimony that the extracts produced

by Catchpole would be considered by those skilled in the art to be more natural than extracts produced by other methods. Ex. 1006 ¶ 83. Sampalis teaches that administration of krill oil can "significantly reduce dysmenorrhea and the emotional symptoms of premenstrual syndrome and is shown to be significantly more effective for the complete management of premenstrual symptoms compared to omega-3 fish oil." Ex. 1012, Abstract.

Given the benefits recited in Catchpole and Sampalis, we agree with Petitioner that one skilled in the art would have been motivated to create a krill oil composition with higher levels of ether phospholipids as taught by Catchpole and include the krill oil composition in a soft gel capsule as taught by Sampalis. Pet. 33–34.

We also find that one skilled in the art would have had a reasonable expectation of success in creating such a composition. Dr. Tallon has credibly testified that denaturing, extraction, and blending methods were well known in the art at the time of the priority date of the '756 patent. Ex. 1006 ¶ 31. We also credit Dr. Tallon's testimony that

> a POSITA would have known that the relative proportions of krill oil constituents could be varied in predictable ways by applying a single solvent or combination of solvents including super critical fluid extraction to selectively extract specific groups of lipid components based on their different solubility, and by blending these selective extracts in known and predictable ways to produce a desired krill oil composition.

Id.

We address Patent Owner's arguments below.

a. Combining Selective and Non-selective Extraction Techniques

Patent Owner contends that one skilled in the art would have concluded that the triglyceride range obtained by a non-selective extraction

method such as that described in Fricke could not be substituted or combined with the ether phospholipid or non-ether phospholipid ranges obtained with the selective extraction process of Catchpole. PO Resp. 17. Patent Owner asserts that the ranges obtained by the different methods are not interchangeable. *Id.* Patent Owner argues that Catchpole and Breivik use different selective extraction methods and that Fricke uses a non-selective extraction method resulting in different lipid profiles for each method. *Id.* at 17–20. For example, Patent Owner contends that the extraction process of Catchpole would have produced a composition where all the triglycerides have been removed. *Id.* at 20. Patent Owner argues that the different processes cannot be combined to produce a krill oil composition with the profile defined by the claims. *Id.* at 20–22.

Petitioner responds that Patent Owner's process arguments are irrelevant as the claims are directed to a krill oil composition and not the method for making it. Reply 5–7. Petitioner contends that based on the teachings of Catchpole and Fricke, one skilled in the art could create a krill oil composition meeting the requirements of the claims. *Id.* at 6. Petitioner argues that although the art teaches the use of different extraction techniques, one skilled in the art would have known how to manipulate the different techniques to obtain the desired lipid profile. *Id.* at 12.

With respect to Catchpole, Petitioner contends that Patent Owner's assertion that the process used in Catchpole would have resulted in zero triglycerides is in error. Reply 8–9. Relying on the testimony of Dr. Tallon, Petitioner asserts that one skilled in the art would have appreciated that not all of the triglycerides would have been removed. *Id.* (citing Ex. 1086 ¶¶ 25–46). Petitioner also contends that Tanaka discloses a process similar

to that in Catchpole, which results in a composition with significant amounts of triglycerides and astaxanthin esters. Reply 9.

In the Sur-Reply, Patent Owner contends that the lipid ranges recited in Fricke and Catchpole are not interchangeable because of the different process used in the two references. Sur-Reply 2–3. Patent Owner reiterates its earlier argument that the method of Catchpole would result in removal of all of the triglycerides and that the process cannot be modified to increase the level of triglycerides without reducing the level of ether phospholipids. *Id.* at 4–5.

Patent Owner also contends that Dr. Tallon's analysis that triglycerides are present in the extract of Catchpole is flawed in that the triglyceride amounts reported in Fricke and used by Dr. Tallon are for the raw material used in Fricke. Sur-Reply 4–5. Patent Owner contends that a proper analysis should have used the triglyceride level from the finished product of Fricke, which would have resulted in a lower calculated level of triglyceride. *Id.*

We begin by noting that the claims of the '765 patent are directed to krill oil compositions and not the methods for making the compositions. *See, e.g.*, Ex. 1001, col. 34, l. 64. Thus, the issues are whether one skilled in the art would have been motivated to create the claimed krill oil composition and whether one skilled in the art would have had a reasonable expectation of success in creating the claimed compositions.

Patent Owner contends that one skilled in the art would not combine the triglyceride range obtained by the non-selective extraction process of Fricke with the ether phospholipid process of Catchpole as the ranges of lipids obtained are not interchangeable. PO Resp. 16–17. Specifically, Patent Owner asserts that the two-step extraction process used in Catchpole

would result in an extract where all of the neutral lipids, such as triglycerides, have been removed. *Id.* We do not read Catchpole so narrowly. Rather, we find that an ordinarily skilled artisan would have understood Catchpole as teaching that a CO_2 extraction step can be used to vary the neutral lipid composition of the extract. Our finding is supported by Catchpole's express disclosure that "[t]he feed material can be processed using pure CO2 before the co-solvent is introduced to remove much or all of neutral lipids," thereby enriching soluble phospholipid content. Ex. 1009, 11. It is further buttressed by Dr. Tallon's testimony that an ordinarily skilled artisan would have understood that the

> relative proportions of krill oil constituents could be varied in predictable ways by applying a single solvent or combination of solvents including super critical fluid extraction to selectively extract specific groups of lipid components based on their different solubility, and by blending these selective extracts in known and predictable ways to produce a desired krill oil composition.

Ex. 1006 ¶ 31. On this record, we credit Dr. Tallon's testimony, as it is consistent with the teachings of the prior art.

In addition, the evidence of record supports the conclusion that Extract 2 of Catchpole contained a significant amount of triglycerides. Table 16 of Catchpole contains 53.7% other compounds. Ex. 1009, 24. Dr. Tallon has credibly testified that, based on his calculations, the other materials would include a significant amount of triglycerides. Ex. 1006 ¶ 46. For example, Breivik teaches the use of a CO_2 and ethanol extraction process that results in an extract containing phospholipids, triglycerides, and astaxanthin. *See, e.g.*, Ex. 1037, 7–9.

Moreover, we credit Dr. Tallon's testimony that triglyceride levels can be adjusted by blending additional triglycerides extracted separately from krill. Ex. 1006 ¶ 282. Dr. Tallon testified that

> a POSITA would have known that the relative proportions of krill oil constituents could be varied in predictable ways by applying a single solvent or combination of solvents including super critical fluid extraction to selectively extract specific groups of lipid components based on their different solubility, and by blending these selective extracts in known and predictable ways to produce a desired krill oil composition. These denaturation, extraction and blending methods were well known to the POSITA prior to the earliest priority date to which the '765 Patent is entitled.

Id. ¶ 31. As discussed more fully below, the present Specifications supports Dr. Tallon's opinion that one skilled in the art would have known how to prepare and blend different fractions together to produce the desired level of triglycerides.

Patent Owner's challenge of Dr. Tallon's triglyceride calculations does not alter our conclusion. As noted above, Breivik teaches that significant amounts of triglycerides are present after CO_2 extraction.

Patent Owner contends that one skilled in the art would have understood that to achieve the desired levels of triglycerides, one would need to add triglycerides to Extract 2 of Catchpole. Sur-Reply 6. Patent Owner contends that this would reduce the amount of ether phospholipid present to less than 4.8%, falling outside the scope of the claims. *Id.*

We find this argument unpersuasive. As Dr. Tallon has testified, one skilled in the art would have understood how to achieve the desired levels of components by selectively extracting the different components and blending the extracts in "known and predictable ways to produce a desired krill oil

composition." Ex. 1006 ¶ 31; *see also* ¶ 53 ("blending can be used to manage the characteristics of the final krill oil compositions") and ¶ 173 ("by blending of different krill oils a composition in the range required by the '765 patent is a simple matter to produce").

Patent Owner's assertion is also belied by the teachings of the '765 patent itself. The Specification of the '765 patent teaches that the compositions of the invention can be prepared by "blending the neutral and polar lipid extracts." Ex. 1001, col. 12, ll. 34–35. The Specification provides no further guidance regarding the blending step but instead relies on the knowledge of those skilled in the art. This supports Dr. Tallon's conclusion that one skilled in the art would have known how to combine the different lipid fractions to achieve the claimed composition.

Accordingly, we are not persuaded that one skilled in the art would not have combined the teachings of the references to produce the claimed compositions.

b. Platelet Activating Factor

Patent Owner also contends that one skilled in the art would have been discouraged from making a krill oil composition for oral ingestion as the ether lipids contained in the composition would have been converted to inflammatory Platelet Activating Factor (PAF). PO Resp. 22–23.

Patent Owner also contends that an ordinarily skilled artisan would not have had reason to use Catchpole's high ether phospholipid containing krill extract to treat conditions associated with inflammation, such as PMS, as taught by Sampalis, because "the prior art taught that dietary ether lipids such as those found in krill could, after being ingested, be converted by peroxidation after ingestion to potent inflammatory Platelet Activating Factor (PAF)." *Id.* at 23 (citing Ex. 2001 ¶ 55). Patent Owner further

argues that one skilled in the art would have been directed away from using the claimed levels of ether phospholipids." *Id.* Specifically, Patent Owner asserts orally administered phosphatidylcholine is almost completely absorbed by the small intestine and appears in the blood stream. *Id.* at 24 (citing Ex. 2001 ¶ 57; Ex. 2008, 1001). Patent Owner contends that the absorbed phosphatidylcholine can be converted to PAF as it was known that phospholipids could be a source of PAFs. *Id.* Patent Owner acknowledges that the art discusses ether-linked glycerol molecules as the source of PAF, Dr. Hoem opines that the same concerns would apply to the ether phospholipids. *Id.* (Ex. 2001 ¶ 57).

Patent Owner also contends that one skilled in the art at the time the invention was made would have understood that oral administration of ether phospholipids was a health concern. *Id.* at 25. Patent Owner points to the teachings of Marathe, who suggests that "rare ether-linked phospholipids in LDL are the likely source of PAF-like activity in oxidized LDL." *Id.* at 25 (citing Ex. 2011, 1). Patent Owner also points to the teaching of Tanaka where foods such as krill "that are rich in 1-O-alkyl-2- ocosahexaenoyl-sn-glycero-3-phosphocholine are potential sources of compounds with high PAF-like activity formed by deleterious lipid peroxidation." PO Resp. 25 (citing Ex. 1014, 1389). Patent Owner contends that one skilled in the art would not have combined the teachings of Sampalis with the references teaching a high level of ether phospholipids such as Catchpole. *Id.* at 26.

Petitioner responds by asserting that Patent Owner's argument that one skilled in the art would not have increased ether phospholipids in krill oil compositions because concerns regarding them being converted into PAFs is unfounded. Reply 13. Petitioner contends that the arguments

presented by Patent Owner are essentially the same as those rejected by the Board in the IPRs 2017-00745 and 2017-00746. *Id.* at 14.

Petitioner contends that the ether phospholipids found in krill oil are chemically distinct from the phospholipids thought to form PAFs. *Id.* at 14–15. Petitioner contends that PAF activity has only been shown to exist for phospholipids having an acyl group with 1–4 carbons. *Id.* at 15 (citing Ex. 2003, 431–432). Petitioner contends that the evidence of record shows that the ether phospholipids found in krill oil have 14–25 carbons. *Id.* (citing Ex. 1086 ¶¶ 55–62). Petitioner asserts that "Prescott teaches that ether phospholipids having longer acyl groups, such as those present in krill and krill oil, would not exhibit PAF activity." *Id.* (citing Ex. 2008, 431–432).

Petitioner also contends that Patent Owner has produced no evidence that ether phospholipids are actually degraded to PAF once ingested. Reply 16–17.

Petitioner asserts that the evidence suggests that there was no real world concern that the ether phospholipids in krill oil would lead to the formation of PAFs. Reply 18. Petitioner cites to the testimony of Dr. Hoem that the ether phospholipid levels of a commercial krill product were considered high. *Id.* (citing Ex. 1090, 54–55, 58). Petitioner contends that there was no concern in the art that the ether phospholipids would lead to PAF formation. *Id.* (citing Ex. 1075).

Petitioner contends that the four additional references cited by Patent Owner do not dictate a different result. Reply 19. Petitioner contends that the study reported in Blank dealt with structurally different phospholipids and that Blank stated that whether dietary phospholipids would create PAF in humans is unknown. *Id.* at 19–20.

Petitioner asserts that neither Zierenberg nor Hartvigsen relates to ether phospholipids and that Marathe discusses oxidation of short-chain alkylphospatidycholines. *Id.* at 20. Petitioner contends that Marathe actually supports Petitioner's position, noting that Marathe teaches "The PAF receptor shows a several hundredfold selectively for the sn-1 ether bond of PAF, and complete specificity for the sn-2 acetyl residue compared with the long chain fatty acyl residue of most alkyl phosphatidylcholines." *Id.* at 10 (quoting Ex. 1094, 1096)

Patent Owner contends in its Sur-Reply that, at the time the invention was made, one skilled in the art would have understood that the ingestion of ether phospholipids could result in the formation of PAF. Sur-Reply 8–9. Patent Owner cites to the testimony of Dr. Tallon, where he acknowledges that the references cited by Patent Owner describe the possible formation of PAF from certain dietary ether phospholipids and that Marathe teaches that peroxidated ether phospholipids in low density lipoprotein ("LDL") can generate an inflammatory response in vivo. *Id.* Patent Owner contends that this supports its contention that the teachings of the art would have lead away from increasing phospholipid levels. *Id.*

Patent Owner also argues that Petitioner's reliance on Patent Owner's GRAS[20] statement is inappropriate in that the GRAS statement was submitted well after the effective filing date of the '765 patent *Id.*

Central to Patent Owner's position is the assertion that "dietary ether phospholipids such as those found in krill, could, after being ingested, be converted by peroxidation after ingestion to potent inflammatory Platelet Activating Factor (PAF)." PO Resp. 22. Neither Patent Owner, nor its

[20] Generally Recognized As Safe.

declarant, Dr. Hoem, however, provides evidence or argument sufficient to support that assertion. Rather, the record reveals that the ether phospholipids of Catchpole are not the same compounds as PAF or PAF-like lipids, and Patent Owner has not adduced evidence or set forth argument adequate to support its contention that the ether phospholipids of Catchpole exhibit PAF-like activity. In addition, the prior art fails to draw any connection between the dietary intake of krill ether phospholipids and the production of PAF or PAF-like lipids or activity such as inflammation.

PAF and the PAF-like compounds Patent Owner characterizes as exhibiting pro-inflammatory activity are structurally and functionally distinct from the ether phospholipids present in Catchpole's krill extract, which do not exhibit PAF-like behavior. As Prescott, one of the references relied upon by Patent Owner as teaching away from the combination of Catchpole and Sampalis, explains, PAF-like activity typically exists only where the acyl group of the phospholipid is in the range of 1–4 carbon atoms:

> The PAF receptor recognizes the *sn*-1 ether bond of PAF, its short *sn*-2 acetyl residue, and the choline head group; alteration of any of these structures greatly decreases signaling through the PAF receptor. Extension of the *sn*-2 acetyl residue by one methylene is without consequence, but extension by two methylenes decreases activity by a factor of 10- to 100-fold, depending on the assay. Extension beyond this results in the loss of signaling through the PAF receptor.

Ex. 2003, 13 (citations omitted). In contrast, as evidenced by the '765 patent and Tanaka, another of the references relied upon to support Patent Owner's teaching away argument, the natural range of acyl groups in krill oil AAPC is from 14 to 25 carbon atoms. Ex. 1001, Table 23; Ex. 1014, 2. Accordingly, we credit Dr. Tallon's testimony that "the effect of the longer

chains (i.e., the 14–24 carbons) essentially removes any concern about PAF and PAF-like activity." Ex. 1086 ¶ 62.

Moreover, at best, Prescott, Tanaka, and Zimmerman, three of the teaching away references cited by Patent Owner, suggest the possible formation of peroxidation products from dietary ether phospholipids under artificial conditions, and disclose that certain of those artificially generated products are similar enough to PAF to trigger the same inflammatory effects. Critically, however, none of these references draws a link between the artificial oxidation of natural ether phospholipids present in krill, and the in vivo signaling behavior of krill ether phospholipids.

For example, Prescott reports that although the artificial "[o]xidation of complex lipids in reduced systems has defined potential oxidation pathways and products, . . . whether such oxidizing conditions exist in vivo is problematic, given the unstable nature of the reactive intermediates and the potential of metabolism of the oxidation products." Ex. 2003, 14.

Similarly, Tanaka, which "investigated the PAF-like lipids formed during peroxidation of PCs from hen egg yolk, salmon roe, sea urchin eggs, and krill in an [*in vitro*] FeSO4/EDTA/ascorbate system" (Ex. 1014, 1), recognizes that "the occurrence of PAF-like lipids in some stored foods is still speculative and requires further investigation" (*id.* at 5). In addition, as Dr. Tallon observes, "[t]he results reported by Tanaka [] apply equally to artificial degradation products of ether phospholipids from general food products such as hen egg yolk, which were and continue to be widely and safely consumed by humans." Ex. 1086 ¶ 28.

Zimmerman, a review article, includes a discussion of the possible production of oxidized phospholipids that exhibit PAF-like activity, but like Prescott and Tanaka, discloses only the artificial generation of such

products, and does not attempt to link dietary intake of natural ether phospholipids and the activity of the potential degradation products described. Ex. 2004, 4–5.

Marathe similarly does not support Patent Owner's argument. Like the other references relied upon by Patent Owner, Marathe focuses on short-chain alkyl phosphatidylcholines and oxidized low density lipoproteins. Ex. 2011, Abstract. In addition, Marathe teaches, "The PAF receptor shows a several hundredfold selectivity for the sn-1 ether bond of PAF, and complete specificity for the sn-2 acetyl residue compared with the long chain fatty acyl residue of most alkyl phosphatidylcholines (5, 6)." Ex. 2011, 11095. This supports Petitioner's assertion that Marathe actually teaches that the ether phospholipids in krill oil would not act like PAF molecules. Ex. 1086 ¶ 56.

Furthermore, the record suggests that an ordinarily skilled artisan would not have been concerned about PAF-like activity arising from dietary ether phospholipid supplementation because the quantity of PAF-like lipids produced, even through the artificial oxidation processes described in the prior art, is quite small. For example, Prescott discloses that only "[s]ome of the many phospholipid oxidation products contain the same features of PAF" (Ex. 2003, 11), and highlights the "unstable nature of the reactive intermediates and the potential of metabolism of the oxidation products" (*id.* at 14), which may lead to the degradation of any PAF-like lipids generated *in vivo*. In addition, Tanaka teaches that the proportion of the artificially produced ether phospholipid oxidation products represents a small proportion of the ether phospholipid starting material. Ex. 1014, 5 ("[T]he yields of 1-*O*-hexadecyl-2-propionyl-GPC and 1-*O*-hexadecyl-2-butyryl-

GPC were 0.0035% and 0.0049% (or 0.0076%), respectively, of the starting krill PC.").

We also observe that the commercial realities at the time of invention of the '765 patent do not support Patent Owner's contention that an ordinarily skilled artisan would have sought to avoid using krill oil extracts having "high" ether phospholipid levels as a dietary supplement. Dr. Hoem testified at deposition that "high" or "substantial" levels of ether phospholipids were essentially any levels that could be quantified. Ex. 1090, 58:10–20; *see also id.* at 54:16–55:10 (characterizing "substantial levels" as "[d]ifferent from trace levels," i.e., levels that could be quantified). Notably, Dr. Hoem also testified that commercially available NKO, which was on sale prior to the invention of the '765 patent (Ex. 1090, 61:9–12), and which the '765 patent identifies as including 2.46% ether phospholipids (Ex. 1001, Table 22), had a "substantial or high" level of ether phospholipids. Ex. 1090, 59:2–61:12. Nevertheless, the record is devoid of evidence suggesting any concern relating to potential harm from the ether phospholipids present in NKO, or any other commercially available prior art krill oil extract. To the contrary, the evidence of record demonstrates that NKO was generally recognized as safe (*see* Ex. 1075; Ex. 1091). Indeed, Patent Owner itself relied on the prior art clinical studies of NKO reported by Sampalis to establish that its own krill oil product was safe. Ex. 1089, 19; Ex. 1090, 52:10–16. Furthermore, although the '765 patent highlights the potential of the disclosed krill oil to reduce inflammation (*see, e.g.*, Ex. 1001, Abstract), it nowhere mentions that such result is unexpected or different from what was achieved by prior art krill oil products. *Cf.* Ex. 1001, col. 11, ll. 34–41 ("The krill oils of the present invention also have unexpected and superior properties as compared to previously available krill

oils. [They have] been demonstrated to reduce blood LDL cholesterol levels, improve DHA transfer to the brain as well as reduce lipid accumulation in the liver and muscle while the previously described krill oil compositions do not have such [] properties.").

Accordingly, we are not persuaded that an ordinarily skilled artisan would have expected krill oil having the ether phospholipid content reported by Catchpole to cause inflammation as Patent Owner contends. Nor do we agree that Prescott, Tanaka, Zimmerman, and/or Marathe teach away from the combination of Sampalis, Catchpole, Fricke, and Breivik.

2. Greater Than About 5% Ether Phospholipids

Claims 18–20, 42–44, and 47 all contain the limitation that the krill oil composition contains greater than about 5% w/w ether phospholipids. As discussed above, for purposes of this decision, we have construed the term "greater than about 5% w/w phospholipids" to include 4.5% w/w phospholipids.

Petitioner contends that Catchpole teaches the preparations of krill oil compositions having 4.8% ether phospholipids. Pet. 31. In support of this contention, Petitioner points to Table 16 of Catchpole, which reports the phospholipid analysis of the feed used to prepare a krill oil extract as well as the extract itself and the residue from the extraction process. *Id.* Table 16 is reproduced below.

Table 16

	Yield % of feed	Composition, %							
		PC	PI	PS	PE	CL	AAPC	AAPE	Other compounds
Feed		6.6	0.0	0.0	0.4	0.1	0.6	0.1	78.6
Extract 2	4.3	39.8	0.0	0.0	0.3	0.2	4.6	0.2	53.7
Residue	79.2	3.6	0.0	0.0	0.3	0.2	0.5	0.1	93.4

Ex. 1009, 24, Table 16.

Dr. Tallon testified that the extract reported in Table 16 contained 4.6% AAPC (alkylacylphosphatidylcholine) and 0.2% AAPE (alkylacylphosphatidylethanolamine), both of which are ether phospholipids. (Ex. 1006 ¶¶ 145, 146, and 282).

Petitioner contends that based on the teaching of Catchpole, it would have been obvious to one of ordinary skill in the art to prepare a krill oil composition having greater than about 5% w/w ether phospholipids. Pet. 37–38.

Relying on its proposed claim construction, Patent Owner contends that Catchpole does not teach a krill oil composition having greater than about 5% w/w ether phospholipids in that 4.8% is less than 4.95%. PO Resp. 27.

Patent Owner also argues that one skilled in the art would not have been motivated to prepare a krill oil composition having greater than about 5% w/w phospholipids as Catchpole does not teach preparing compositions having a higher amount of phospholipids and such a composition cannot be prepared by the method disclosed in Catchpole. *Id.*

In response, Petitioner argues that even if Patent Owner's proposed claim construction were correct, Catchpole still teaches preparation of krill oil compositions having greater than about 5% w/w ether phospholipids. Reply 25.

Petitioner begins by arguing that Table 16 only reports the weight percentages for two of the phospholipids that are present in krill oil. *Id.* Petitioner contends that one skilled in the art would have recognized that a third phospholipid, lyso-alkylacylphosphatidylcholine (LAAPC), would also be present in an amount of at least 0.4%, thereby bringing the total phospholipid content to 5.2%. *Id.* In support of this argument, Petitioner

cites to the testimony of Dr. Tallon, who calculates that the level of LAAPC would be about 0.4% based on the data reported in Table 22 of Catchpole. Ex. 1086 ¶ 196.

Petitioner also argues that Catchpole specifically teaches preparing extracts with greater than about 5% w/w ether phospholipids. Reply 25–27. In particular, Petitioner points to the portion of Catchpole where it teaches "More preferably the product contains greater than 5% acylalkyphospholipids . . . . Even more preferably the product comprises greater than 10% acylalkyphospholipids." Reply 25; Ex. 1008, 9, ll. 17–21. Petitioner also contends that Catchpole specifically claims composition having greater than 5% acylalkyphospholipids. Reply 27–28.

Based on our review of the record as a whole, we determine that a preponderance of the evidence supports Petitioner's contention that an ordinarily skilled artisan would have been motivated to create a krill oil composition containing greater than about 5% w/w phospholipids. As discussed above, Catchpole and Sampalis teach the health benefits of krill oil and specifically phospholipids. Ex. 1009, 1; Ex. 1012, Abstract. In addition, Catchpole specifically teaches a preference for compositions containing greater than 5% by weight acylalkyphospholipids. Ex. 1009, 9. We find that the teachings of Catchpole and Sampalis would have motivated one skilled in the art to create a krill oil composition having greater than 5% by weight ether phospholipids.

As discussed above, we have construed the term "about 5%" to include values as low as 4.5%. As Petitioner has demonstrated, Table 16 of Catchpole teaches a krill oil composition having 4.8% ether phospholipids. Ex. 1009, 24. Thus Catchpole teaches a krill oil composition having "about" 5% ether phospholipids.

Regarding Patent Owner's argument with respect to Catchpole not teaching a composition having greater than about 5% w/w phospholipids, the record indicates that Catchpole teaches that higher levels of phospholipids are desirable. Ex. 1009, 9. Thus, although Catchpole might not contain a specific example of a krill oil composition having in excess of 5% ether phospholipids, Catchpole teaches that it is desirable to prepare such a composition. As Dr. Tallon has testified, one skilled in the art would have been able to create such a composition using conventional extraction techniques. Ex. 1006 ¶ 31.

Based on the foregoing, therefore, we determine that Petitioner has established by a preponderance of the evidence that claims 1–4, 7, 9–11, 14, 18–20, 25–28, 31, 33–35, 38. 42–44, and 47 of the '765 patent are unpatentable over the combination of Catchpole, Sampalis, Fricke and Breivik.

F. Obviousness Based on Sampalis, Catchpole, Fricke, Breivik, and Bottino

Petitioner asserts that claims 5, 6, 12, 13, 15, 16, 21–23, 29, 30, 36, 37, 39, 40, 45, and 46 are unpatentable under 35 U.S.C. § 103(a) as obvious over Sampalis, Catchpole, Fricke, Breivik, and Bottino. Pet. 47–55.

Claims 5, 12, 15, 21, 29, 36, 39, and 45 further define claims 1, 10, 14, 19, 25, 34, 38, and 43, respectively, specifying that the krill oil composition includes from about 20% to 35% omega-3 fatty acids as a percentage of total fatty acids in the composition. Ex. 1001, col. 35, ll. 12–14, 34–43, 57–59, col. 36, ll. 20–22, 40–43, 50–53, col. 37, ll. 1–4. Petitioner relies on Bottino as teaching this claim requirement, asserting that Bottino discloses a krill oil composition comprising between 25.0% and 30.0% omega-3 fatty acids. Pet. 47–50, 55. Petitioner also asserts that a

person of ordinary skill in the art would have had a reason to combine the omega-3-fatty acid levels taught in Bottino with the encapsulated krill oil disclosed in the combination of references of Ground 1 because of the known significant health benefits of omega-3-fatty acids. Pet. 55 (citing Ex. 1006 ¶¶ 50–54, 314). From the evidence presented, we find that Petitioner has established by a preponderance of the evidence that dependent claims 5, 12, 15, 21, 29, 36, 39, and 45 are unpatentable in view of Sampalis, Catchpole, Sampalis, Fricke, Breivik, and Bottino.

Claim 23 further defines claim 15, specifying that the krill oil includes greater than about 400 mg/kg astaxanthin esters. Ex. 1001, col. 35, ll. 63–65. Petitioner relies on Breivik for a teaching of this requirement. Pet. 50–51. From the evidence presented, we find that Petitioner has established a preponderance of the evidence that dependent claim 23 is unpatentable in view of Sampalis, Catchpole, Sampalis, Fricke, Breivik, and Bottino. *See, e.g.*, Ex. 1006 ¶¶ 177–188.

Claims 6, 13, 16, 22, 30, 37, 40, and 46 further define claims 5, 12, 15, 21, 29, 36, 39, and 45, respectively, specifying that from about 70% to 95% of the omega-3 fatty acids are attached to the phospholipids. Ex. 1001, col. 35, ll. 16–18, 34–36, 44–46, 60–62, col. 36, ll. 24–26, 44–46, 54–56, col. 37, ll. 5–7. Petitioner relies on Fricke and the testimony of Dr. Tallon for a teaching of this requirement. Pet. 51–54. From the evidence presented, we find that Petitioner has established by a preponderance of the evidence that dependent claims 6, 13, 16, 22, 30, 37, 40, and 46 are unpatentable in view of Sampalis, Catchpole, Fricke, Breivik, and Bottino.

Patent Owner does not challenge Petitioner's assertions concerning Bottino's disclosures, or its addition to the combination of Sampalis, Catchpole, Fricke, and Breivik. Rather, Patent Owner argues that the

addition of "Bottino I does not cure the deficiencies noted above for the four core references." PO Resp. 29.

For the reasons set forth above with regard to the asserted ground of unpatentability over Sampalis, Catchpole, Fricke, and Breivik, however, we do not find Patent Owner's argument persuasive. As previously discussed, we find that an ordinarily skilled artisan would have had reason for, and a reasonable expectation of success in, combining Sampalis, Catchpole, Fricke, and Breivik.

We have reviewed Petitioner's evidence and arguments, which we adopt as our own, and determine that Petitioner has established that the claims are rendered obvious by the combination of Sampalis, Catchpole, Fricke, Breivik, and Bottino. *See*, *e.g.*, Ex. 1006 ¶¶ 307–310.

Accordingly, we determine that Petitioner has established by a preponderance of the evidence that claims 5, 6, 12, 13, 15, 16, 21–23, 29, 30, 36, 37, 39, 40, 45, and 46 of the '765 patent are unpatentable over the combination of Sampalis, Catchpole, Fricke, Breivik, and Bottino.

G. Obviousness Based on Sampalis, Catchpole, Frick, Breivik, and Randolph.

Claims 8, 17, 24, 32, 41, and 48 further define claims 1, 11, 19, 25, and 43, respectively, specifying that the krill oil includes a plant phytonutrient. Ex. 1001, col. 35, ll. 21–22, 47–48, 66–67, col. 36, ll. 29–30, 57–58, col. 37, ll. 11–12. Petitioner relies on Randolph for a teaching of this requirement, asserting that Randolph discloses a composition comprising a phytonutrient and krill oil. Pet. 56–60. Petitioner further asserts that a person of ordinary skill in the art would have had a reason to combine a phytonutrient as taught by Randolph in the krill oil composition taught by the Sampalis, Catchpole, Fricke, Breivik in an oral administration form as

taught by Sampalis and Randolph because Randolph teaches the health benefits of compositions that include both krill oil and phytonutrients. *Id.* at 59–60 (citing Ex. 1006 ¶¶ 50–54, 200–203, 322–323).

Patent Owner does not challenge Petitioner's assertions concerning Randolph's disclosures, or its addition to the combination of Sampalis, Catchpole, Fricke, and Breivik. Rather, Patent Owner argues that the addition of Randolph to the combination does not address the defects of the four core references. PO Resp.30.

For the reasons set forth above with regard to the asserted ground of unpatentability over Sampalis, Catchpole, Fricke, and Breivik, however, we do not find Patent Owner's argument persuasive. As previously discussed, we find that an ordinarily skilled artisan would have had reason for, and a reasonable expectation of success in combining Sampalis, Catchpole, Fricke, and Breivik.

We have reviewed Petitioner's evidence and arguments, which we adopt as our own, and determine that Petitioner has established that claims 8, 17, 24, 32, 41, and 48 are rendered obvious by the combination of Catchpole, Sampalis, and Randolph. *See, e.g.*, Ex. 1006 ¶¶ 77, 78, 316–323.

Accordingly, we determine that Petitioner has established by a preponderance of the evidence that claims 8, 17, 24, 32, 41, and 48 of the '765 patent are unpatentable over the combination of Sampalis, Catchpole, Fricke, Breivik and Randolph.

III. PATENT OWNER'S MOTION TO AMEND

Patent Owner's motion to amend is contingent on the Board's finding of unpatentability of the challenged claims. MTA 1. Because we conclude that Petitioner has demonstrated that the challenged claims are unpatentable,

we proceed to consider Patent Owner's motion to substitute claims 46–52 for claims 25–32. For the reasons discussed below, Patent Owner's motion to amend is denied.

A. Threshold Requirements

In an *inter partes* review, claims may be added as part of a proposed motion to amend. 35 U.S.C. § 316(d). The Board must assess the patentability of the proposed substitute claims "without placing the burden of persuasion on the patent owner." *Aqua Prods., Inc. v. Matal*, 872 F.3d 1290, 1328 (Fed. Cir. 2017) (en banc). Patent Owner's proposed substitute claims, however, must still meet the statutory requirements of 35 U.S.C. § 316(d) and the procedural requirements of 37 C.F.R. § 42.121 as a threshold matter. *See* USPTO's Memorandum, Guidance On Motions to Amend in view of *Aqua Products* (Nov. 2017), available at https://www.uspto.gov/sites/default/files/documents/guidance_on_motions_to_amend_11_2017.pdf. Accordingly, Patent Owner must demonstrate: (1) the amendment proposes a reasonable number of substitute claims; (2) the amendment does not seek to enlarge the scope of the claims of the patent or introduce new subject matter; (3) the amendment responds to a ground of unpatentability involved in the trial; and (4) the original disclosure sets forth written description support for each proposed claim. *See* 35 U.S.C. § 316(d)(1)(B),(3); 37 C.F.R. § 42.121; *Hospira, Inc. v. Genentech, Inc.*, Case IPR2017-00737, slip op. at 47 (PTAB Oct. 3, 2018) (Paper 108).

B. Proposed Substitute Claims

Proposed substitute claims 49 to 56 are reproduced below with markings showing proposed changes from claims 25 to 32, respectively. Deletions are shown in brackets and additions are underlined.

Proposed Claim 49. (Proposed substitute claim in place of original claim 25.) Encapsulated krill oil comprising:

a capsule containing a safe and effective amount of *E. superba* krill oil, said krill oil comprising greater than [about 3%] from 5% to 8% ether phospholipids w/w of said krill oil; from about 27% to 50% non-ether phospholipids w/w of said krill oil so that the amount of total phospholipids in the composition is from about 30% to 60% w/w of said krill oil; from about 20% to 50% triglycerides w/w of said krill oil, and astaxanthin esters in amount of [greater than about] from 100 mg/kg to 700 mg/kg of said krill oil.

Proposed Claim 50. (Proposed substitute claim in place of original claim 26.) The encapsulated krill oil of claim [25] 49, wherein said krill oil in said capsules contains [greater than about] from 200 mg/kg to 700 mg/kg astaxanthin esters.

Proposed Claim 51. (Proposed substitute claim in place of original claim 27.) The encapsulated krill oil of claim [25] 50, wherein said krill oil in said capsules contains [greater than about] from 300 mg/kg to 700 mg/kg astaxanthin esters.

Proposed Claim 52. (Proposed substitute claim in place of original claim 28.) The encapsulated krill oil of claim [25] 51, wherein said krill oil in said capsules contains [greater than about] from 400 mg/kg to 700 mg/kg astaxanthin esters.

Proposed Claim 53. (Proposed substitute claim in place of original claim 29.) The encapsulated krill oil of claim [25] 52, wherein said krill oil in said capsules comprises from about 20% to 35% omega-3 fatty acids as a percentage of total fatty acids in said composition.

Proposed Claim 54. (Proposed substitute claim in place of original claim 30.) The encapsulated krill oil of claim [25] 53, wherein from about 70% to 95% of said omega-3 fatty acids are attached to said phospholipids.

Proposed Claim 55. (Proposed substitute claim in place of original claim 31.) The encapsulated krill oil of claim [25] 54, wherein said capsule is a soft gel capsule.

> Proposed Claim 56. (Proposed substitute claim in place of original claim 32.) The encapsulated krill oil of claim [25] 55, wherein said capsule further contains a plant phytonutrient.

MTA, App'x A.

C. Broadening, Definiteness, and Written Description

We construe only those terms that are in controversy, and only to the extent necessary to resolve the controversy. *See Vivid Techs*., Inc. v. Am. Sci. Engr., Inc, 200 F.3d 795, 803 (Fed. Cir. 1999); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co*., 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review). None of the newly added claim terms are in controversy, so no claim construction is required.

In particular, for the reasons discussed below, we determine that the substitute claims do not broaden the invention and that substitute claims 49–56 are definite and have adequate written description support.

1. The Substitute Claims Do Not Broaden the Scope of the Claims.

Proposed claim 49 removes the term "greater than about" and adds an upper limit of 8% by weight for the ether phospholipid present in the krill oil composition and removed the term "greater than about" and adds an upper limit of 700 mg for the amount of astaxanthin present in the krill oil composition. Dependent claims 50–52 add the upper limit of 700 mg to the astaxanthin amounts recited in the claims. These changes narrow the amounts of ether phospholipids and astaxanthin present in the krill oil composition and do not broaden the scope of the claims.

2. The Substitute Claims Are Not Indefinite

As with the original claims, the terms recited in the substitute claims are well understood by those skilled in the art. We find that the claims are definite.

3. The Substitute Claims Are Supported by the Specification

Patent Owner contends that the added limitations of from 5% to 8% ether phospholipids and from 100 to 700 mg astaxanthin are supported by the present Specification and find support in U.S. Patent Application No. 14/020,155 ("the '155 Appl."). MTA 3–7. Patent Owner contends that both the '155 Appl. and the present Specification teach that the krill oil compositions of the invention may comprise "from about 1%, 2%, 3% or 4% to about 8%, 10%, 12% or 15% w/w ether phospholipids or greater than about 4%, 5%, 6%, 7%, 8%, 9% or 10% ether phospholipids." Ex. 2012, 15; MTA 5. Patent Owner also contends that the present examples support this limitation, especially Example 7. MTA 5.

Similarly, Patent Owner contends that the present Specification and the '155 Appl. support the upper limit of astaxanthin. MTA 7–8. Both the '155 Appl. and the Specification teach, "in some embodiments, the krill oil compositions comprise greater than about 100, 200, 300, 400, or 500 mg/kg astaxanthin esters and up to about 700 mg/kg astaxanthin esters." Ex. 2012, 16–17; *see also* Ex. 2012, Tables 17C, 19C, and 20C.

Petitioner does not contest that the Specification and the '155 Appl. provide written support for the amended claim limitations.

Based on the foregoing, we conclude that the new claim limitations are supported by the Specification and do not introduce new matter.

D. Unpatentability

Petitioner asserts that the proposed substitute claims 49–56 are unpatentable under 35 U.S.C. § 103(a). MTA Opp. 1. Petitioner contends that the subject matter of substitute claims 49–52, 55, and 56 would have been obvious to one of ordinary skill in the art over Sampalis combined with Catchpole, Fricke and NKO.[21] *Id.* at 20. Petitioner contends that the subject matter of claims 53 and 54 would have been obvious over Sampalis combined with Catchpole, Fricke, Bottino, and NKO. *Id.* at 23. Finally Petitioner contends that the subject matter of claim 56 would have been obvious over Sampalis combined with Catchpole, Fricke, Randolph, and NKO. *Id.* at 24. To support its Opposition, Petitioner offers the declaration of Dr. Tallon. Patent Owner disagrees. MTA Reply 1–12. Patent Owner relies on the deposition of Dr. Tallon. Ex. 2020.

We determine that claims 49–52, 55, and 56 would have been obvious over the combination of Sampalis, Catchpole, Fricke, and NKO. We determine that claims 53 and 54 would have been obvious over the combination of Sampalis, Catchpole, Fricke, Bottino, and NKO. We determine that claim 56 would have been obvious over the combination of Sampalis, Catchpole, Fricke, Randolph, and NKO.

In support of its contention that the substitute claims would have been obvious, Petitioner reiterates the arguments discussed above and presents new arguments addressing the amended elements relating to the amount of ether phospholipids and astaxanthin esters. As with the original claims, Patent Owner's response focuses on the issues of motivation to combine and

[21] NKO refers to Neptune Krill Oil referenced in Sampalis, Ex. 1012, 4, and described as prior art in the present Specification, Ex. 1001, col. 27, ll. 38–50.

reasonable expectation of success. Patent Owner also addresses the amended limitations regarding ether phospholipids and astaxanthin esters. We shall focus our discussion on these issues.

1. *From 5% to 8% Ether Phospholipids*

Petitioner asserts that the limitation of from 5% to 8% ether phospholipids would have been obvious over the teachings of Catchpole. MTA Opp. 4. In support of this contention, Petitioner again points to Table 16 of Catchpole, which reports levels of ether phospholipids of 4.8 %. *Id.* at 3. Petitioner also relies on the testimony of Dr. Tallon, where he states that one skilled in the art would have understood that the remainder reported in Table 16 would include at least 0.4% LAAC, thereby bringing the total ether phospholipids to 5.2%, i.e., within the range recited in the substitute claims. *Id.* at 5–6; Ex. 1086 ¶ 196.

Petitioner also argues that the Specification recites a broad range of ether phospholipids amounts and does not attribute any criticality to the range of from 5% to 8%. MTA Opp. 5. Petitioner contends that given the difference between 4.8% and 5%, there is no basis for asserting that the recited range is critical. *Id.*

Catchpole expressly discloses krill oil compositions having greater than 5% ether phospholipids. *Id.* at 12. In support of this contention, Petitioner again points to the passage in Catchpole where it teaches that compositions of the invention preferable have greater that 5% acylalkylphospholipids. *Id.* at 13; Ex, 1009, 9. Petitioner also points to the claims of Catchpole, which claim compositions having greater than 5% ether phospholipids. MTA Opp. 13–14.

Patent Owner responds by asserting that the substitute claims delete the term “about” and should be interpreted as meaning that the claims are

limited to amounts of ether phospholipids greater than 5%. MTA 13–14. Patent Owner contends that Catchpole does not teach or suggest a krill oil composition having greater than 5%. *Id.* Patent Owner argues that at best Catchpole teaches a krill oil composition having 4.8% ether phospholipids, which is well below 5%. *Id.* at 14. Patent Owner contends that one skilled in the art would have been discouraged from using a higher amount of ether phospholipids because the art teaches that higher amounts of ether phospholipids can create potent PAF analogs, which could cause inflammation. *Id.* at 14–15.

Patent Owner also contends that Dr. Tallon's calculation of the amount of LAAC present in Catchpole was not publically available information and the calculation rests on several improper assumptions, including where the LAAC was present in the extract prepared in Catchpole and the relative amounts of the reported ether phospholipids. MTA Reply 3–4.

Patent Owner also contends that the level of ether phospholipid could not be easily adjusted as suggested by Dr. Tallon. *Id.* at 4–5. Patent Owner contends that adjusting one component of the krill oil composition would necessarily result in a change in the amounts of the other components. *Id.* For example, Patent Owner argues that using the extraction process of Catchpole would result in removing all of the neutral lipids such as triglycerides from the composition. *Id.* Patent Owner argues that Dr. Tallon's own calculations support this conclusion. *Id.* at 6–7. Patent Owner also points to the teaching in Catchpole where it states that "The feed material can be processed using pure CO2 before the co-solvent is introduced to remove much or all of the neutral lipids." Ex. 1009, 13; MTA Reply 6. Patent Owner also points to the statement in Example 18 of

Catchpole where it states that the CO_2 extraction was performed "until no further extract was obtained." MTA Reply 7; Ex. 1009, 24. Patent Owner contends that in order to create a composition having the requisite amount of triglycerides, one skilled in the art would need to add triglycerides to the composition resulting in a dilution of ether phospholipids. MTA Reply 7; Ex. 1009, 24.

Patent Owner argues that the recited ranges are critical and that it would require more than routine optimization to prepare the claimed compositions. MTA Reply 8. Patent Owner supports this contention by noting that the composition reported in Example 18 of Catchpole does not contain triglycerides and that triglycerides would need to be added to the composition. *Id.* Patent Owner contends that adding triglycerides to the composition would result in decreasing the weight percent of ether phospholipids to well below 5%. Patent Owner contends that Catchpole does not teach how greater than 5% ether phospholipids could be achieved. *Id.*

With respect to the reference to acylalkylphospholipids being present in amounts greater than 5%, Patent Owner points out that the cited portion of Catchpole actually refers to acylalkylphospholipids and/or plasmilogens and not ether phospholipids alone. *Id.* at 9. Patent Owner contends that this does not teach preparing a krill oil composition with 5% to 8% ether phospholipids. *Id.*

Patent Owner also contends that Dr. Tallon's use of the triglyceride levels of Fricke in his calculation of residual triglycerides was improper in that Dr. Tallon used the triglyceride levels of the krill oil before extraction. *Id.* at 9. Patent Owner contends that a comparison of the triglyceride level of Fricke with Extract 2 of Catchpole is improper because Fricke reports

triglyceride levels for whole krill, which is comparable to the feed material of Example 18 of Catchpole and not the product after extraction. *Id.* Patent Owner contends that one skilled in the art would not have combined the references as suggested by Petitioner. *Id.*

Patent Owner reiterates its argument that one skilled in the art would not have been motivated to increase the ether phospholipid levels in a krill oil composition because the ether phospholipids might be converted into PAF-like compounds and cause inflammation. *Id.* at 10–11. Patent Owner argues that Petitioner improperly relied on Patent Owner's GRAS statement as the statement and the studies reported therein are all dated after the effective filing date of the '765 patent. *Id.*

In its Sur-Reply, Petitioner argues that Dr. Tallon testified that Extract 2 of Catchpole does contain LAAC and that the amount of LAAC calculated by Dr. Tallon is correct. MTA Sur-Reply 2–3. Petitioner contends that any error in Dr. Tallon's calculation was an honest mistake and that the error does not detract from Dr. Tallon's conclusion that the Extract in Catchpole contained LAAC. *Id.* Dr. Tallon, a co-inventor of Catchpole, explained why LAAC was not listed as one of the components in Table 16 and why LAAC would be included in the amount of extract not accounted for in Table 16.

Petitioner also contends that the amounts of ether phospholipids in the composition can be easily adjusted. MTA Sur-Reply 3–7. Petitioner argues that Patent Owner's assertion that triglycerides would need to be added to the extract of Catchpole is based on an erroneous assumption. *Id.* Petitioner contends that the extract of Catchpole would contain triglycerides as stated by Dr. Tallon in his declaration. *Id.* at 3. Petitioner argues that the calculations Dr. Tallon performed during his cross-examination used an

incorrect assumption as to the initial amount of triglycerides present in the starting material and that this is the basis for Patent Owner's assertion that the resulting extract contained no triglycerides. *Id.* at 4. Petitioner contends that when the proper value is used the results show that approximately 115 grams of triglyceride remain in the extract. *Id.*

Petitioner also contends that Catchpole does not teach that all triglycerides are removed by the initial step of the extraction process but actually teach that the parameters of the extraction process can be adjusted so as to yield the desired amounts of the different constituents. MTA Sur-Reply 6. For example, in Examples 7 and 8, Catchpole teaches that the percentage of phospholipids can be increased by altering the polar solvent concentration. *Id.*

Petitioner also contends that, when read as a whole, Catchpole teaches ether phospholipid levels of greater that 5%. MTA Sur-Reply 7. Petitioner asserts that Catchpole teaches methods for separating lipids from marine animals, including krill, and teaches that the process can result in ether phospholipid levels greater that 5%. *Id.*

Petitioner also asserts that Patent Owner's argument regarding the ether phospholipids forming PAF-line materials is without merit. MTA Sur-Reply 7–8. Petitioner contends that the additional art cited by Patent Owner does not teach that the peroxidation occurs in vivo but only reports in vitro and does not refute the evidence that the phospholipids recovered from krill oil are structurally and functionally different that those reported to have PAF –like activity. *Id.* Petitioner also asserts that Patent Owner's GRAS filing relied on studies published before the filing of the patent making it relevant. *Id.* at 8. Finally, Petitioner points out that Patent Owner's argument is

contradicted by statements in the '765 patent that the krill oil compositions are anti-inflammatory. *Id.* at 9.

Viewed as a whole, we determine that a preponderance of the evidence demonstrates that it would have been obvious to one of ordinary skill in the art to prepare a krill oil composition having from greater than 5% to 8% ether phospholipids. The evidence also demonstrates that one skilled in the art would have been motivated to increase the ether phospholipid levels to enhance the health benefits of the resulting krill oil composition and would have had a reasonable expectation of success.

Catchpole teaches the preparation of compositions having greater than 5% acylalkylphospholipids. Ex. 1009, 9. Although we agree with Patent Owner that the cited passage in Catchpole also refers to plasmalogens, the use of the connector "and/or" teaches that the compositions can include only acylalkylphospholipids. *Id.* In addition, the claims of Catchpole also teach compositions having greater than 5% acylalkylphospholipids. Ex. 1009, 35, claim 95.

As discussed above, Catchpole also teaches a krill oil extract having at least 4.8% ether phospholipid, which is adjacent to the range recited in the substitute claims.[22] Ex. 1009, 24, Table 16. Given the closeness of the value reported in Catchpole and the recited range, one skilled in the art would expect them to have the same properties, absent evidence to the contrary. *See* Ex. 1006 ¶ 195 (stating that a small change in composition would not affect properties); *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir.

[22] We do not address Petitioner's contention that one skilled in the art would recognize that the composition in Catchpole would actually comprise 5.2% ether phospholipids as the overall teaching of Catchpole supports a finding of obviousness.

2003). We find no evidence in the record that compositions falling within the range recited in the substitute claims possess different properties than the composition disclosed in Catchpole.

Given the overall teachings of Catchpole that an acylalkylphospholipid level of greater than 5% is preferred and the teaching of a specific example adjacent to the claimed range, we conclude that it would have been obvious to prepare a krill oil composition having from greater than 5% to 8% ether phospholipids.

We have considered Patent Owner's arguments regarding a lack of motivation to combine the references and lack of a reasonable expectation of success and we agree with Petitioner that they are merely a reiteration of the arguments addressed above. For the reasons discussed above, we find these arguments unpersuasive.

a. Astaxanthin Esters in an Amount of from 100 mg/kg to 700 mg/kg of Said Krill Oil

Substitute claim 49 adds an upper limit to the amount of astaxanthin esters present of 700mg/kg. Patent Owner contends that one skilled in the art would not have been motivated to prepare a krill oil composition with this amount of astaxanthin esters as the art teaches compositions having in excess of 1000 mg/kg. MTA 17–20. Specifically Patent Owner asserts that Breivik and Randolph each teach krill oil compositions having significantly more than 700 mg/kg astaxanthin esters. *Id.* Patent Owner also contends that the higher level of astaxanthin esters taught in Breivik and Randolph constitute teachings away from the range recited in the substitute claims. *Id.*

Petitioner responds by asserting that the present Specification discloses that a prior art krill oil composition, NKO, contains 472 mg/kg of astaxanthin ester. MTA Opp. 15. Petitioner also asserts that Randolph

teaches that the disclosed krill oil compositions can have "any amount of an astaxanthin" and that Randolph does not teach away from the use of lower astaxanthin esters. *Id.* at 15–16.

In reply, Patent Owner asserts that one skilled in the art would not have known that the astaxanthin ester content of NKO was 472 mg/kg when the GRAS statement for NKO teaches that the composition contains 1500 mg/kg. MTA Reply 11. Patent Owner argues that obviousness cannot be predicated on what was not known to one skilled in the art. *Id.*

In its Sur-Reply, Petitioner asserts that Patent Owner has admitted that the NKO product is prior art and that it can properly be considered in the obviousness analysis. MTA Sur-Reply 9. In addition, Petitioner contends that Randolph teaches a krill oil composition having between 100 mg/kg and 700 mg/kg of astaxanthin ester. *Id.* In support of this contention, Petitioner relies on the testimony of Dr. Tallon where he opines that one skilled in the art would have understood that Randolph discloses a krill oil composition having 158 mg/kg of astaxanthin ester. MTA Sur-Reply 10 (citing Ex. 2020, 155:11–157:2).

Viewed as a whole, we determine that a preponderance of the evidence demonstrates that it would have been obvious to one of ordinary skill in the art to prepare a krill oil composition having from greater than 100mg/kg to 700mg/kg astaxanthin esters.

We begin with the admitted prior art of the NKO product. Although we agree with Petitioner that the sample tested by Patent Owner shows an astaxanthin ester level of 472 mg/kg, we are not persuaded that the subject matter of the claims would have been obvious based on that evidence.

Petitioner's argument is premised on the proposition that the NKO product would inherently have an astaxanthin level with the range recited in

the substitute claims. Although inherency may be used to support a conclusion of obviousness, our reviewing court has warned that the use of inherency in an obviousness context "must be carefully circumscribed." *PAR Pharm. Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1195 (Fed Cir. 2014). To support a conclusion that a property is inherent, Petitioner must show that the astaxanthin ester level is necessarily present in the NKO product. *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). As Patent Owner has shown, the GRAS statement filed by Neptune[23] lists an astaxanthin ester level of greater than 1500 mg/kg. Ex. 1075, 9–10. Dr. Tallon also testified that, other than the data in the '765 patent, he was not aware of any other analysis of the NKO product that showed astaxanthin levels for the NKO product that were within the range recited in the substitute claims. Ex. 2020, 149–150.

Based on the foregoing we find that Petitioner has failed to establish that the NKO product would inherently have an astaxanthin level of from 100 mg/kg to 700 mg/kg.

We now turn to Randolph. Randolph teaches

> A composition can contain any amount of an astaxanthin ingredient. For example, at least about 1 percent (e.g., at least about 2, 3, 4, 5, 10, 15, 20, 25, 30, 35, 40, 50, 60, 70, 80, or 90 percent) of a dietary supplement can be astaxanthin. Typically, a composition contains between about 0.5 mg and about 50 mg of an astaxanthin ingredient.

Ex. 1011 ¶ 44. Randolph also teaches that the composition typically contains about 300 mg to about 3000 mg of krill oil. *Id.* ¶ 40. Sampalis II[24]

[23] Neptune Technologies & Bioresources ("Neptune")
[24] Sampalis, WO 03/011873 A2, published Feb. 13, 2003 ("Sampalis II") (Ex. 1013).

teaches that the astaxanthin in krill oil is mainly present as esterified astaxanthin. Ex. 1013. Dr. Tallon testified that, assuming that 95% of the astaxanthin present in the composition of Randolph is esterified, the amount of astaxanthin ester ranges as low as 158 mg/kg. Ex. 2020, 155–157.

Based on the foregoing, we conclude that it would have been obvious to one of ordinary skill in the art to prepare a krill oil composition with between 100 mg/kg and 700 mg/kg of astaxanthin esters. Although we agree with Patent Owner that Randolph's teaching of percentages ranging from 1% and higher would lead to an astaxanthin level greater than 1000 mg/kg, as demonstrated above, when read as a whole, Randolph teaches lower amounts that overlap with the range recited in the substitute claims. "A prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003).

We conclude that substitute claims 49–52, 55, and 56 would have been obvious over the combination of Sampalis, Catchpole, Fricke, and NKO. We conclude that substitute claims 53 and 54 would have been obvious over the combination of Sampalis, Catchpole, Fricke, Bottino, and NKO. We conclude that substitute claim 56 would have been obvious over the combination of Sampalis, Catchpole Fricke, Randolph, and NKO.

III. CONCLUSION

We conclude that Petitioner has shown by a preponderance of the evidence that (1) claims 1–4, 7, 9–11, 14, 18–20, 25–28, 31, 33–35, 38, 42–44, and 46 are unpatentable over the combination of Sampalis, Catchpole, Fricke and Breivik, (2) claims 5, 6, 12, 13, 15, 16, 21–23, 29, 30, 36, 37, 39, 40, 45, and 46 are unpatentable over the combination of Sampalis, Catchpole, Fricke, Breivik, and Bottino, and (3) claims 8, 17, 24, 32, 41, and 48 are unpatentable over the combination of Sampalis, Catchpole, Fricke, Breivik and Randolph.

We deny Patent Owner's contingent Motion to Amend to replace claims 25–32 with substitute claims 49–56, as those claims are unpatentable over the cited prior art.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED, based on a preponderance of the evidence that claims 1–48 of the '765 are unpatentable;

FURTHER ORDERED, Patent Owner's Motion to Amend is denied as to replacing claims 25–32 with substitute claims 49–56; and

FURTHER ORDERED, because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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